U.S. FOOD & DRUG ADMINISTRATION

March 13, 2020

Siri & Glimstad LLP
Aaron Siri, Esq.
200 Park Avenue 17th Floor
New York, NY 10166

In reply refer to file: F18-7308

Dear Mr. Siri,

This is in reply to your Freedom of Information Act request dated September 7, 2018, in which you requested "A copy of the report for each clinical trial relied upon by the FDA when approving FluLaval for six month old babies." Your request was received in the Center for Biologics Evaluation and Research on September 12, 2018.

Enclosed are the records that our search located.

We have withheld portions of pages under Exemption (b)(6), 5 U.S.C. § 522(b)(6). That exemption protects information from disclosure when its release would cause a clearly unwarranted invasion of personal privacy. FOIA Exemption 6 is available to protect information in personnel or medical files and similar files. This requires a balancing of the public's right to disclosure against the individual's right to privacy.

You have the right to appeal this determination. By filing an appeal, you preserve your rights under FOIA and give the agency a chance to review and reconsider your request and the agency's decision.

Your appeal must be mailed within 90 days from the date of this response to:

Deputy Agency Chief FOIA Officer
U.S. Department of Health and Human Services
Office of the Assistant Secretary for Public Affairs
Room 729H
200 Independence Avenue, S.W.
Washington, DC 20201
E-mail: FOIARequest@PSC.hhs.gov

Please clearly mark both the envelope and your letter or email "**FDA** Freedom of Information Act Appeal."

If you would like to discuss our response before filing an appeal to attempt to resolve your dispute without going through the appeals process, please contact:

Beth Brockner Ryan, Branch Chief
Center for Biologics Evaluation and Research (CBER)
Access Litigation and Freedom of Information Branch
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Building 71, Room 1114
Silver Spring, MD 20993-0002
E-mail: beth.brocknerryan@fda.hhs.gov
Main Line: 240-402-7800
FOI Line: 240-402-8008

You also have the right to contact:

FDA FOIA Public Liaison
Office of the Executive Secretariat
5630 Fishers Lane
Room-1050
Rockville, MD 20857
E-mail: FDAFOIA@fda.hhs.gov

If you are unable to resolve your FOIA dispute through our FOIA Public Liaison, the Office of Government Information Services (OGIS), the Federal FOIA Ombudsman's office, offers mediation services to help resolve disputes between FOIA requesters and Federal agencies. The contact information for OGIS is:

Office of Government Information Services
National Archives and Records Administration
8601 Adelphi Road–OGIS
College Park, MD 20740-6001
Telephone: 202-741-5770
Toll-Free: 1-877-684-6448
Fax: 202-741-5769
E-mail: ogis@nara.gov

If you have any questions or if we can be of further assistance, please let us know by referencing the above file number. You can contact Elizabeth Sly by phone at 240-402-8001 or by e-mail at Elizabeth.Sly@fda.hhs.gov.

Sincerely,

Beth A. Brockner Ryan -S

Digitally signed by Beth A. Brockner Ryan -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300052489, cn=Beth A. Brockner Ryan -S
Date: 2020.03.13 13:41:36 -04'00'

Beth Brockner Ryan
Chief, Access Litigation and Freedom of Information Branch

GlaxoSmithKline Biologicals

Study title

Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) when administered in children.

Study detailed title

A phase III, double blind, randomized study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to GSK Biologicals' trivalent influenza vaccine *Fluarix*® administered intramuscularly to children 3 to17 years of age; and to describe the safety and immunogenicity of GSK2282512A in children 6-35 months of age.

Clinical Study Report for Study: 113314 (FLU Q-QIV-003 PRI)

(Development Phase III)

IND Number: 14466

Indication Studied: Immunization against influenza in male and female subjects 3-17 years of age, inclusive.

Study initiation date:	01-October 2010
Study completion date:	06-July 2011
Data lock point:	03-October 2011
Date of report:	Amendment 1 Final: 28-June 2012
Earlier Study Reports:	Final: 01-December 2011

Sponsor Signatory: Varsha K. Jain, MD,
Director, Global Vaccine Development, Influenza Vaccines, GlaxoSmithKline Biologicals

This study was performed in compliance with Good Clinical Practice including the archiving of essential documents.

GSK Biologicals' Study Report INS-BIO-CLIN-1010 v02

SYNOPSIS

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Title of the study : A phase III, double blind, randomized study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to GSK Biologicals' trivalent influenza vaccine *Fluarix*® administered intramuscularly to children 3 to17 years of age; and to describe the safety and immunogenicity of GSK2282512A in children 6-35 months of age.

Principal investigators: This study was conducted by 32 principal investigators across five countries (Canada, Mexico, Spain, Taiwan, and the United States).

Study centers: This was a multi-center study conducted at 32 centers across Canada, Mexico, Spain, Taiwan, and the United States.

Publication (reference): Not published as of 28-June-2012

Study period: Study initiation date: 01-October 2010 Study completion date: 06-July 2011 Data lock point: 03-October 2011	**Clinical phase: III**

Objectives:

Primary:

- To test the immunogenic non-inferiority (in terms of Geometric Mean Titer [GMT] and Seroconversion Rate [SCR]) for the shared viral strains of FLU Q-QIV versus *Fluarix*-VB (TIV containing Victoria B strain) and *Fluarix*-YB (TIV containing Yamagata B strain) in children 3 to 17 years old approximately 28 days after completion of dosing (approximately at Day 28 for primed subjects and approximately at Day 56 for unprimed subjects).

  Criteria (based on FDA/CBER guidance) to conclude non-inferiority:
  The test of non-inferiority was based on the analysis of the entire 3 to 17 year-old age range in each treatment group, and immunogenic non-inferiority was concluded if:
  - The upper limit of the two-sided 95% confidence interval of the GMT ratio (*Fluarix*/FLU Q-QIV) after completion of the vaccination series did not exceed 1.5 for the three strains (H3N2, H1N1 and shared B, i.e., VB or YB), AND
  - The upper limit of the two-sided 95% confidence interval for the difference in SCR (*Fluarix* minus FLU Q-QIV) did not exceed 10% for the three strains contained in each *Fluarix* vaccine (TIV-VB and TIV-YB)

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Objectives (continued):

Secondary:

- To test the immunogenic superiority of the B strains present in FLU Q-QIV (in terms of GMT ratio and SCR) in children 3 to 17 years old approximately 28 days after completion of dosing (approximately at Day 28 for primed subjects; approximately at Day 56 for unprimed subjects) by comparing:
  - FLU Q-QIV to *Fluarix*-YB (i.e., TIV-YB) with respect to the Victoria lineage B strain, and
  - FLU Q-QIV to *Fluarix*-VB (i.e., TIV-VB) with respect to the Yamagata lineage B strain

  Criteria to conclude superiority:
  - The test of immunogenic superiority was based on the analysis of the entire 3 to 17 year-old age range in each treatment group, and immunogenic superiority was concluded if the lower limit of the two-sided 95% confidence interval on GMT ratio (FLU Q-QIV/*Fluarix*) was greater than 1.5 and the difference in SCR (FLU Q-QIV minus *Fluarix*) was greater than 10%.

- To describe the immunogenicity (in terms of Geometric Mean Titer [GMT], seroprotection rate [SPR], seroconversion rate [SCR] and seroconversion factor [SCF]) of FLU Q-QIV and each *Fluarix* vaccine overall, and for the age categories 3 to 8 years and 9 to 17 years, and of FLU-Q-QIV for the 6-35 month age group.
- To evaluate fulfilment of CBER immunogenicity criteria by the immune response to the second, Yamagata lineage, B strain in FLU Q-QIV (in 3-17 year olds).
  (FDA/CBER criteria were considered met if the lower limit of 95% CI for SCR was ≥40% and post-vaccination SPR was ≥70%).
- To evaluate and describe the reactogenicity and safety of FLU Q-QIV and each *Fluarix* vaccine overall in the 3 to 17 years age category and for the age categories 3 to 8 years and 9 to 17 years. The reactogenicity and safety of FLU-Q-QIV for the 6-35 month age group were also described.
  The following reactogenicity and safety analyses were performed:
  - Solicited local symptoms during the 7-day post-vaccination follow-up (day of vaccination and 6 subsequent days) overall (3-17 years) and in three age groups (6 to 35 months, 3-8 years, 9-17 years).
  - Solicited general symptoms during the 7-day post-vaccination follow-up (day of vaccination and 6 subsequent days) overall (3-17 years), and for the 6 to 35 months, 3 to 4 year, 5 to 8 year and 9 to 17 year-old age groups (note that the 3-4 year-old and 5-8 year-old groups are assessed using different solicited general symptoms because of their differential reporting abilities, and are thus analyzed separately for this category).
  - Unsolicited symptoms during the 28-day (day of vaccination and 27 subsequent days) post-vaccination follow-up period overall (3-17 years), and in the 6 to 35 months, 3-8 years and 9-17 years age groups.

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

- Serious adverse events (SAEs), medically attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period (Day 0 to Day 180 after the first vaccination), overall (3-17 years), and in the 6 to 35 months, 3-8 years and 9-17 years age groups.

Study design:

- Randomized (1:1:1) in three treatment groups (FLU Q-QIV, *Fluarix*-VB, and *Fluarix*-YB), age stratified (1:1 into 2 age strata, 3-8 years old, and 9-17 years old), multi-center study (multi-country), with a double-blind design for the comparison of FLU Q-QIV to each *Fluarix* TIV in 3 to 17 year-old subjects and open-label for the descriptive evaluation of FLU Q-QIV in 6 to 35 month-old subjects (independent and stand alone arm which did not contribute any data to the analysis of the three blinded arms of the study).
- *Vaccination schedule:* One intramuscular (IM) injection at Day 0 for primed subjects and two IM injections, one at Day 0 and one at Day 28 for unprimed subjects.
  - *Primed subjects:* Subjects ≥ 9 years of age and any subjects 6 months to 8 years of age who had received at least one dose of an influenza A [H1N1] 2009 monovalent vaccine in the last season [or had laboratory confirmed H1N1 infection] AND have received two doses of seasonal influenza vaccine separated by at least one month during the last season or had received at least one dose prior to last season.
  - *Unprimed subjects:* Subjects 6 months to 8 years of age who had not received any influenza A [H1N1] 2009 monovalent vaccine in the previous season [or did not have laboratory confirmed H1N1 infection] OR who had not received any seasonal influenza vaccine in the past or received only one dose for the first time in the last influenza season.
- *Immunogenicity sampling:* Blood samples were collected at Days 0 and 28 for primed subjects and Days 0 and 56 for unprimed subjects.

Number of subjects:

- *Planned:*
  - Total: **3000**; QIV1: **900**; TIV-VB: **900**; TIV-YB: **900**; QIV2: **300**
- *Enrolled:*
  - Total: **3109**; QIV1: **932**; TIV-VB: **929**; TIV-YB: **932**; QIV2: **302**; Not vaccinated: **15**
- *Total vaccinated cohort, TVC (Safety analysis):*
  - Total: **3094**; QIV1: **932**; TIV-VB: **929**; TIV-YB: **932**; QIV2: **301**
- *ATP Immunogenicity cohort, ATP-I (Immunogenicity analysis):*
  - Total: **2886**; QIV1: **878**; TIV-VB: **871**; TIV-YB: **878**; QIV2: **259**
- *Completed (6-month Safety follow up):*
  - Total: **2960**; QIV1: **894**; TIV-VB: **889**; TIV-YB: **902**; QIV2: **275**

QIV1=FLU Q-QIV (3-17 years of age), **TIV-VB**=*Fluarix*-VB (3-17 years of age);
TIV-YB=*Fluarix*-YB (3-17 years of age); **QIV2**=FLU Q-QIV (6-35 months of age)

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Diagnosis and criteria for inclusion:

Male or female children 6 months to 17 years of age who were in stable health at the time of the first vaccination (health status as determined by investigator's clinical examination and assessment of subjects' medical history).

Study vaccine, dose, mode of administration, lot no.:

FLU Q-QIV vaccine:

- *Vaccination schedule /site:* FLU Q-QIV vaccine administered at Visit 1 (Day 0) for primed and unprimed subjects and a 2nd dose at Visit 2 (Day 28), only for unprimed subjects. Vaccine was given intramuscularly (IM) in the deltoid muscle of the non-dominant arm to children ≥12 months of age and in the anterolateral region of the thigh to infants <12 months of age.
- *Vaccine composition /dose /lot number:* HA from 4 influenza strains (total HA/0.5 mL dose = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage).
- *Lot numbers:* DFLHA585A (initial lot, expiry date of 21-Dec-2010) and DFLHA642A (re-supply lot with a longer expiry date, 20-Mar-2011, in order to allow recruitment of additional subjects).

Reference vaccine /Comparator, dose and mode of administration, lot no.:

***Fluarix*-VB (TIV-VB) vaccine:**

- *Vaccination schedule /site:* TIV-VB vaccine administered at Visit 1 (Day 0) for primed and unprimed subjects and a 2nd dose at Visit 2 (Day 28), only for unprimed subjects. Vaccine was given intramuscularly (IM) in the deltoid muscle of the non-dominant arm (in subjects 3 to 17 years of age).
- *Vaccine composition /dose /lot number:* HA from 3 influenza strains (total HA/0.5 mL dose = 45 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria-lineage).
- *Lot number:* AFLUA521A (expiry date: 31-May-2011).

***Fluarix*-YB (TIV-YB) vaccine:**

- *Vaccination schedule /site:* TIV-YB vaccine administered at Visit 1 (Day 0) for primed and unprimed subjects and a 2nd dose at Visit 2 (Day 28), only for unprimed subjects. Vaccine was given intramuscularly (IM) in the deltoid muscle of the non-dominant arm (in subjects 3 to 17 years of age).
- *Vaccine composition /dose /lot number:* HA from 3 influenza strains (total HA/0.5 mL dose = 45 µg, 15 µg each strain): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/3/2007 (Yamagata lineage).
- *Lot number:* DFLUA039A (expiry date: 30-Jun-2011).

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Duration of treatment:
Approximately 4 - 8 weeks to complete enrolment and approximately 6 months for each enrolled subject to complete study.

Endpoints:

- *Immunogenicity*:

  Humoral immune response to each of the influenza vaccine strains in each vaccine group (FLU Q-QIV and each TIV in 3-17 year olds). Measurement of serum Hemagglutination Inhibiting (HI) antibody titer against each strain at pre-vaccination (Day 0) and at post-vaccination (Day 28 for primed or Day 56 for unprimed subjects).

  - Primary endpoints included the following parameters (with 95% confidence intervals [CIs]) which were calculated for all subjects in each treatment group: GMTs of HI antibody titers and SCRs for each strain at Day 28 after the last vaccine dose in each treatment group.

  - Secondary endpoints to further assess humoral immune response included the following parameters (with 95% CIs) which were calculated for all subjects and for the 6 to 35 months, 3-8 years and 9-17 years old age groups: Geometric mean reciprocal serum HI antibody titers and SPRs against each of the vaccine strains in each group at Day 0 and at Day 28 after the last vaccine dose, and SCRs and SCFs for the vaccine strains at Day 28 after the last vaccine dose in each treatment group.

- *Safety/reactogenicity*:

  – Recording of incidence rate, duration, and intensity of solicited local adverse events (pain, redness, and swelling at injection site for all subjects) during a 7-day follow-up period (Day 0 to Day 6) after each vaccination in each treatment group.

  – Recording of incidence rate, duration, intensity, and relationship to vaccination of solicited general adverse events (fever, irritability/fussiness, drowsiness, loss of appetite in subjects <5 years of age and fatigue/tiredness, fever, headache, joint pain, generalized/widespread muscle aches, and shivering in subjects ≥5 years of age) during a 7-day follow-up period (Day 0 to Day 6) after each vaccination in each treatment group.

  – Recording of incidence rate, intensity, and relationship to vaccination of unsolicited adverse events during a 28-day follow-up (Day 0 to Day 27) after each vaccination in each treatment group.

  – Recording of Serious Adverse Events (SAEs), Medically Attended Adverse Events (MAEs), and potential immune-mediated diseases (pIMDs) in each treatment group during the entire study period (i.e, day of first vaccination and 180 subsequent days).

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Statistical methods:

- Analyses were performed as per protocol:

- *Demographic characteristics* (age, gender, and ethnicity/geographic ancestry) were analyzed for each study cohort. The mean age (in years) with range and standard deviation and the mean age by gender of the vaccinated cohort, as a whole, and by group, were calculated. The proportion of subjects with prior immunologic experience with influenza vaccine(s) in the previous three seasons (i.e., history of influenza vaccination) were tabulated for each treatment group by two categories: subjects with no prior immunization and subjects with prior exposure.

- *Analysis of immunogenicity* was performed on the ATP cohort (primary analysis) and on the Total vaccinated cohort (complementary analysis). GMT ratios and SCR difference with their 95% CI were calculated for each strain in the entire age range at Day 28 following last vaccination. For each vaccine strain, GMT of HI antibodies, SCRs, SPRs, and SCFs were calculated for each treatment group for all subjects and also by the three age groups (6 to 35 months, 3-8 years, and 9-17 years old).

- *Analysis of safety/reactogenicity* was performed on the Total vaccinated cohort. Incidences of adverse events (solicited local, solicited general, and unsolicited), with 95% CI, were calculated for each treatment group for all subjects and also by the three age groups (6 to 35 months, 3-8 years, and 9-17 years old). MAEs, SAEs, pIMDs, and withdrawals due to an AE were collected and summarized through the entire six month safety follow-up period. The incidences of concomitant medication and concomitant vaccinations were also tabulated.

Summary of Study Results:

- *Demography (Total vaccinated cohort):*

The demographic profiles were comparable across the three treatment groups (QIV1, TIV-VB, and TIV-YB in subjects 3 to 17 years old) with respect to mean age, gender and racial distribution. The mean age of subjects was 8.9 years in each treatment group. In total, 51.6% of subjects were male and 48.4 % were female. The population was predominantly White/Caucasian (62.8%). For the QIV2 group (6 to 35 months of age), the mean age of subjects was 1.2 years. In total, 52.5% of subjects were male and 47.5 % were female. The population was predominantly White/Caucasian (68.4%).

- *Immunogenicity:*

The immunogenicity analyses were performed on the ATP cohort (primary analysis) and on the Total vaccinated cohort (supplemental analysis) since the percentage of vaccinated subjects eliminated (6.7%) from the ATP cohort exceeded 5%.

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Summary of Study Results: (continued)

The results of the immunogenicity analyses showed that:

- The study met its confirmatory primary objective of demonstrating immunogenic non-inferiority of the quadrivalent FLU Q-QIV vaccine compared to the trivalent *Fluarix* vaccines, TIV-VB (*Fluarix* containing Victoria B strain) or TIV-YB (*Fluarix* containing Yamagata B strain) after completion of the vaccination series in children 3 to 17 years of age. Both pre-defined statistical acceptance criteria for concluding immunogenic non-inferiority of all four strains in the FLU Q-QIV vaccine were met:
  - the upper limit of the two-sided 95% confidence interval (CI) of the adjusted GMT ratio (*Fluarix*/FLU Q-QIV) was ≤ 1.5 for each strain (A/H3N2, A/H1N1, VB and YB) contained in the FLU Q-QIV vaccine *and*,
  - the upper limit of the two-sided 95% CI for the difference in SCR (*Fluarix* minus FLU Q-QIV) was ≤ 10% for each strain (A/H3N2, A/H1N1, VB and YB) contained in the FLU Q-QIV vaccine.
- The study met the confirmatory secondary objective of demonstrating immunogenic superiority of the quadrivalent FLU Q-QIV vaccine over the trivalent *Fluarix* vaccines, TIV-VB (with respect to the *Yamagata* lineage B strain) and TIV-YB (with respect to the *Victoria* lineage B strain) after completion of the vaccination series in children 3 to 17 years of age. Both pre-defined statistical acceptance criteria for inferring immunogenic superiority of QIV vs TIVs for the unique B strain in the QIV vs TIVs were met:
  - the lower limit of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) was > 1.5 with respect to the B strain present in QIV but absent from the *Fluarix*-TIV (VB or YB) in the specific QIV to TIV comparison (i.e., Q-QIV vs TIV-VB or TIV-YB) *and*
  - the lower limit of the two-sided 95% CI for the difference in SCR (FLU Q-QIV minus *Fluarix*) was > 10% with respect to the B strain present in QIV but absent from the *Fluarix*-TIV (VB or YB) in the specific QIV to TIV comparison (i.e., Q-QIV vs TIV-VB or TIV-YB).
- The study also achieved its confirmatory secondary objective of meeting CBER criteria for the additional B strain in the FLU Q-QIV vaccine administered to children 3 to 17 years of age. The immunogenic response to the alternate, Yamagata-lineage, B strain in FLU Q-QIV fulfilled CBER's immunogenicity criteria (lower limit of 95% CI for SCR ≥40% and lower limit of 95% CI for post-vaccination seroprotection rate [SPR] ≥70%) predictive of clinical benefit.
- The descriptive immunogenicity data (GMT, SCR, SPR, and SCF) indicated that, in children 6 to 35 months of age, each of the four strains in the FLU Q-QIV vaccine met CBER's SPR and SCR criteria (lower limit of 95% CI for SCR ≥40% and post-vaccination seroprotection rate [SPR] ≥70%) indicative of clinical benefit, with the exception of the SPR for A/Victoria/210/2009 (H3N2) strain (LL of 95% CI for SPR=68.8%).

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Summary of Study Results: *Immunogenicity (continued):*

Synopsis Table 1. Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) and *Fluarix*-YB (TIV-YB) in terms of adjusted GMT ratios of HI antibody post-last vaccination for eachof the four QIV strains (non-inferiority criterion: adjusted GMT ratio UL of 95% CI ≤ 1.5) (ATP-I)

Antibody	TIV-VB+TIV-YB		QIV1		Adjusted GMT ratio (TIV-VB+TIV-YB / QIV1)		
						95% CI	
	N	Adj GMT	N	Adjusted GMT	Value	LL	UL
A/California/7/2009 (H1N1)	1747	421.4	876	366.3	1.15	1.06	**1.25**
A/Victoria/210/2009 (H3N2)	1746	144.3	876	145.8	0.99	0.92	**1.07**

Antibody	TIV-VB		QIV1		Adjusted GMT ratio (TIV-VB / QIV1)		
						95% CI	
	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
B/Brisbane/60/2008 (Victoria)	870	243.4	876	252.5	0.96	0.87	**1.07**

Antibody	TIV-YB		QIV1		Adjusted GMT ratio (TIV-YB / QIV1)		
						95% CI	
	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
B/Florida/4/2006 (Yamagata)	877	564.6	876	525.2	1.08	0.99	**1.16**

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB+TIV-YB = Pooled TIV Fluarix-VB and Fluarix-YB groups (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Synopsis Table 2. Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) and *Fluarix*-YB (TIV-YB) in terms of seroconversion rate (difference in SCR) at day 28 eachof the four QIV strains (non-inferiority criterion: difference in SCR, UL of 95% CI ≤ 10%) (ATP-I)

Antibody	QIV1			TIV-VB+TIV-YB			Difference in SCR (%) (TIV-VB+TIV-YB minus QIV1)		
								95% CI	
	N	n	SCR (%)	N	n	SCR (%)	%	LL	UL
A/California/7/2009 (H1N1) (1/DIL)	876	739	84.4	1747	1505	86.1	1.79	-1.04	**4.77**
A/Victoria/210/2009 (H3N2) (1/DIL)	876	614	70.1	1746	1200	68.7	-1.36	-5.05	**2.41**

Antibody	QIV1			TIV-VB			Difference in SCR (%) (TIV-VB minus QIV1)		
								95% CI	
	N	n	SCR (%)	N	n	SCR (%)	%	LL	UL
B/Brisbane/60/2008 (Victoria) (1/DIL)	876	653	74.5	870	622	71.5	-3.05	-7.21	**1.12**

Antibody	QIV1			TIV-YB			Difference in SCR (%) (TIV-YB minus QIV1)		
								95% CI	
	N	n	SCR (%)	N	n	SCR (%)	%	LL	UL
B/Florida/4/2006 (Yamagata) (1/DIL)	876	659	75.2	877	644	73.4	-1.80	-5.89	**2.30**

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB+TIV-YB = Pooled TIV Fluarix-VB and Fluarix-YB groups (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years); TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
Seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Synopsis Table 3. Descriptive immunogenicity of FLU Q-QIV, *Fluarix*-VB, and *Fluarix*-YB in terms of GMT, SCR, SPR, and SCF (ATP-I)

			GMT			SCR			SPR			SCF		
				95% CI			95% CI			95% CI			95% CI	
Group	Timing	N	value	LL	UL	%	LL	UL	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)														
QIV1	PRE	876	29.4	26.8	32.2	-	-	-	54.8	51.4	58.1	-	-	-
	POST	878	362.7	335.3	392.3	84.4	**81.8**	86.7	96.8	**95.4**	97.9	12.3	11.3	13.4
TIV-VB	PRE	870	32.2	29.4	35.3	-	-	-	57.0	53.6	60.3	-	-	-
	POST	871	429.1	396.5	464.3	86.8	**84.3**	89.0	97.4	**96.1**	98.3	13.3	12.3	14.4
TIV-YB	PRE	877	29.1	26.6	31.8	-	-	-	54.4	51.0	57.7	-	-	-
	POST	878	420.2	388.8	454.0	85.5	**83.0**	87.8	96.6	**95.2**	97.7	14.4	13.3	15.7
QIV2	PRE	259	16.8	13.9	20.3	-	-	-	33.6	27.9	39.7	-	-	-
	POST	259	200.9	166.6	242.2	84.9	**80.0**	89.1	89.6	**85.2**	93.0	12.0	10.5	13.6
A/Victoria/210/2009 (H3N2)														
QIV1	PRE	876	18.1	16.7	19.7	-	-	-	33.7	30.5	36.9	-	-	-
	POST	878	143.7	134.2	153.9	70.1	**66.9**	73.1	92.9	**91.0**	94.5	7.9	7.3	8.6
TIV-VB	PRE	870	19.0	17.4	20.6	-	-	-	34.6	31.4	37.9	-	-	-
	POST	871	139.6	130.5	149.3	67.8	**64.6**	70.9	92.8	**90.8**	94.4	7.4	6.8	8.0
TIV-YB	PRE	876	19.4	17.8	21.1	-	-	-	37.0	33.8	40.3	-	-	-
	POST	878	151.0	141.0	161.6	69.6	**66.5**	72.7	93.3	**91.4**	94.8	7.8	7.2	8.5
QIV2	PRE	259	5.6	5.3	6.0	-	-	-	2.70	1.1	5.5	-	-	-
	POST	259	61.4	53.8	70.0	73.0	**67.1**	78.3	74.5	**68.8**	79.7	10.9	9.6	12.4
B/Brisbane/60/2008 (Victoria)														
QIV1	PRE	876	24.8	22.5	27.3	-	-	-	44.3	41.0	47.7	-	-	-
	POST	878	250.5	230.8	272.0	74.5	**71.5**	77.4	95.4	**93.8**	96.7	10.1	9.2	11.1
TIV-VB	PRE	870	25.8	23.5	28.4	-	-	-	46.4	43.1	49.8	-	-	-
	POST	871	245.4	226.9	265.4	71.5	**68.4**	74.5	96.3	**94.9**	97.5	9.5	8.6	10.5
TIV-YB	PRE	877	25.8	23.5	28.4	-	-	-	45.6	42.3	49.0	-	-	-
	POST	877	68.1	61.9	74.9	29.9	26.9	33.1	73.3	**70.3**	76.2	2.6	2.5	2.8
QIV2	PRE	259	8.7	7.5	10.0	-	-	-	10.8	7.3	15.2	-	-	-
	POST	259	127.3	109.4	148.1	84.6	**79.6**	88.7	88.0	**83.4**	91.7	14.6	12.8	16.6
B/Florida/4/2006 (Yamagata)														
QIV1	PRE	876	57.9	52.0	64.4	-	-	-	66.0	62.7	69.1	-	-	-
	POST	878	512.5	477.6	549.9	75.2	**72.2**	78.1	99.0	**98.1**	99.5	8.9	8.1	9.7
TIV-VB	PRE	870	58.4	52.6	64.9	-	-	-	67.0	63.8	70.1	-	-	-
	POST	871	197.0	180.7	214.8	41.3	38.0	44.6	92.4	**90.5**	94.1	3.4	3.1	3.6
TIV-YB	PRE	877	65.9	59.3	73.2	-	-	-	70.9	67.8	73.9	-	-	-
	POST	878	579.0	541.2	619.3	73.4	**70.4**	76.3	99.4	**98.7**	99.8	8.8	8.1	9.6
QIV2	PRE	259	7.7	7.0	8.6	-	-	-	8.5	5.4	12.6	-	-	-
	POST	259	192.7	172.1	215.7	93.8	**90.2**	96.4	96.5	**93.5**	98.4	24.9	22.0	28.3

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
GMT = geometric mean antibody titer calculated on all subjects
SCR = seroconversion rate. Seroconversion defined as:
for initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
for initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
SPR (seroprotection rate) = the percentage of vaccinees with a serum HI titer ≥ 1:40
SCF (seroconversion factor) = Fold increase in serum HI GMTs post-vaccination
N = number of subjects with available results (for GMT and SPR)
N = number of subjects with pre- and post-vaccination results available (for SCR and SCF)
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0; POST= Day 28 post last vaccination

Summary of Study Results (continued):

- *Safety /reactogenicity:*

The safety analysis was performed on the Total vaccinated cohort (TVC). Since the percentage of vaccinated subjects excluded from the ATP cohort for analysis of safety (ATP-S) was less than 5% of the TVC, no secondary (complementary) analysis was performed on the ATP-S.

The results of the reactogenicity/safety analyses are summarized below. The overall incidence and nature of solicited and unsolicited adverse events (AEs) are presented in Synopsis Table 4. Data for the solicited local and general AEs, unsolicited AEs and MAEs, and SAEs are summarized here and presented in detail in the body of the report.

- Overall incidence of *solicited and unsolicited* AEs (overall/subject)
  - *Any* solicited and unsolicited AEs were reported for 77.3%, 71.6%, and 69.0% of subjects in the QIV1, TIV-VB, and TIV-YB groups (3-17 years of age), respectively, and for 74.8% of subjects in the QIV2 group (Synopsis Table 4).

- *Solicited local* AEs (overall/subject):
  - Injection site pain was the most frequently reported local AE across all treatment groups with a a lower incidence in children 6-35 months of age (reported for 69.8%, 59.0% and 59.2% of 3-17 year-old subjects in the QIV1, TIV-VB, TIV-YB and 50.3% of 6-35 month-old subjects in the QIV2 groups, respectively).

  - Grade 3 injection site pain was reported for 3.8%, 2.3%, 2.8%, and 2.0% of subjects in the QIV1, TIV-VB, TIV-YB, and QIV2 groups, respectively.

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Summary of Study Results (continued):

- *Solicited general* AEs (overall/subject):
  - Drowsiness (24.9%, 25.1%, and 27.0% of subjects) and irritability (31.9%, 23.5%, and 25.4% of subjects) were the most frequently reported general AEs across the three treatment groups (QIV1, TIV-VB, and TIV-YB groups, respectively) among subjects 3 to 5 years of age. In the QIV2 group (Q-QIV in subjects 6 to 35 months of age), irritability (48.3%) was the most frequently reported general AE, followed by drowsiness (34.9%), and loss of appetite (31.8%).

  - Muscle ache (30.5%, 26.8%, and 26.6% of subjects), fatigue (23.8%, 24.4%, and 24.4% of subjects), and headache (23.4%, 23.6%, and 21.6% of subjects) were the most frequently reported general AEs across the three treatment groups (Q-QIV, TIV-VB, and TIV-YB groups, respectively) in subjects 5 years of age and older.

  - Grade 3 solicited general AEs, including fever, were reported with a very low incidence rate, ranging from 0.0% to 3.2% (in subjects 3 to <5 years of age) and 0.0% to 1.8% (in subjects ≥5 to 17 years of age).

- *Unsolicited AEs and MAEs* (medically-attended adverse events):
  - Among the 3 to 17 year-old subjects, 283 (30.4%) from the QIV1 group, 291 (31.3%) from the TIV-VB group, and 275 (29.5%) from the TIV-YB group reported at least one unsolicited adverse event (AE) during the 28-day post-vaccination period. In the QIV-only, 6 to 35 months old age group (QIV2), 160 subjects (53.2%) reported at least one unsolicited AE during the 28-day post-vaccination period. For all treatments and across both age groups, cough was the most frequently reported AE.

  - Among the 3 to 17 year old subjects, 346 subjects (37.1%) from the QIV1 group, 335 (36.1%) from the TIV-VB group, and 350 (37.6%) from the TIV-YB group reported at least one MAE during the entire study period. In the QIV-only, 6 to 35 months old age group (QIV2), 147 subjects (48.8%) reported at least one MAE during the entire study period. For all treatments and across both age groups, upper respiratory tract infection was the most frequently reported MAE.

- *SAEs* (Serious adverse events):
  - No fatal SAEs were reported during the entire study period. Overall, 35 SAEs were reported in 21 subjects during the entire study period (out of a total vaccinated cohort of 3094 subjects).

  - In subjects 3-17 years of age, two SAEs (angioedema and conjunctivitis) with onset on the day of vaccination reported for one subject (PID (b) (6) a 12-year old male subject) in the *Fluarix*-YB (TIV-YB) group were considered by the investigator to be related to the study vaccination. Both SAEs were reported to have recovered/resolved.

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Summary of Study Results (continued): *SAEs* (Serious adverse events):

- In subjects 6-35 months of age, two SAEs (grand mal convulsion in PID (b) (6), a 1-year old female subject with onset on the day of the first dose of Q-QIV; febrile convulsion in PID (b) (6), a 2-year old male subject with onset 18 days after first dose of Q-QIV) were also considered to be related to vaccination. Both SAEs were reported to have recovered/resolved.

Synopsis Table 4: Incidence and nature of symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (TVC)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	QIV1	932	690	74.0	71.1	76.8	932	453	48.6	45.4	51.9	932	601	64.5	61.3	67.6
	TIV-VB	929	625	67.3	64.2	70.3	929	437	47.0	43.8	50.3	929	506	54.5	51.2	57.7
	TIV-YB	932	619	66.4	63.3	69.4	932	444	47.6	44.4	50.9	932	515	55.3	52.0	58.5
	QIV2	301	206	68.4	62.9	73.7	301	168	55.8	50.0	61.5	301	137	45.5	39.8	51.3
Dose 2	QIV1	331	197	59.5	54.0	64.8	331	112	33.8	28.8	39.2	331	171	51.7	46.1	57.2
	TIV-VB	330	190	57.6	52.0	63.0	330	108	32.7	27.7	38.1	330	155	47.0	41.5	52.5
	TIV-YB	328	171	52.1	46.6	57.7	328	92	28.0	23.3	33.2	328	145	44.2	38.8	49.8
	QIV2	233	131	56.2	49.6	62.7	233	104	44.6	38.1	51.3	233	85	36.5	30.3	43.0
Overall/dose	QIV1	1263	887	70.2	67.6	72.7	1263	565	44.7	42.0	47.5	1263	772	61.1	58.4	63.8
	TIV-VB	1259	815	64.7	62.0	67.4	1259	545	43.3	40.5	46.1	1259	661	52.5	49.7	55.3
	TIV-YB	1260	790	62.7	60.0	65.4	1260	536	42.5	39.8	45.3	1260	660	52.4	49.6	55.2
	QIV2	534	337	63.1	58.9	67.2	534	272	50.9	46.6	55.3	534	222	41.6	37.4	45.9
Overall/subject	QIV1	932	720	77.3	74.4	79.9	932	484	51.9	48.7	55.2	932	642	68.9	65.8	71.8
	TIV-VB	929	665	71.6	68.6	74.5	929	479	51.6	48.3	54.8	929	550	59.2	56.0	62.4
	TIV-YB	932	643	69.0	65.9	72.0	932	470	50.4	47.2	53.7	932	546	58.6	55.3	61.8
	QIV2	301	225	74.8	69.4	79.6	301	193	64.1	58.4	69.5	301	156	51.8	46.0	57.6

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
For each dose: N= number of subjects with at least one administered dose; n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose: N= number of administered doses; n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Name of company: GlaxoSmithKline Biologicals, North America. **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine, FLU Q-QIV (Quebec-manufactured) **Name of active substance:** [HA from 4 influenza strains (total HA/0.5 mL = 60 µg, 15 µg each): A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria-lineage), B/Florida/4/2006 (Yamagata-lineage]	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	(for national authority only)

Summary of Study Results (continued):

- *Withdrawals due to adverse events /serious adverse events:*
  - There were no subject withdrawals due to a serious adverse event.
  - One subject (PID (b) (6) from the QIV2 group (FLU Q-QIV/6-35 months of age) was withdrawn (no Day 180 contact) subsequent to a non-serious adverse event (moderate fever) which was reported as "resolved/recovered." The decision to withdraw from the study was made by the subject's parent(s)/legally acceptable representative(s).
- *Pregnancies:*
  - There was one case of pregnancy (PID (b) (6) reported in this study. The subject was a 17-year old female who received *Fluarix*-VB approximately 2 months before her last menstrual period; the subject was exposed to vaccine prior to conception. After 38 weeks gestation, the subject gave birth to a live male infant by caesarian section due to failure to progress and umbilical cord wrapped around the neck of the fetus.

Overall Conclusions: FLU Q-QIV-003 study

- The study met its confirmatory primary objective of demonstrating immunogenic non-inferiority of the quadrivalent FLU Q-QIV vaccine compared to the trivalent *Fluarix* vaccines, TIV-VB (*Fluarix* containing Victoria B strain) or TIV-YB (*Fluarix* containing Yamagata B strain) after completion of the vaccination series in children 3 to 17 years of age.
- The study met the confirmatory secondary objective of demonstrating immunogenic superiority of the quadrivalent FLU Q-QIV vaccine over the trivalent *Fluarix* vaccines, TIV-VB (with respect to the *Yamagata* lineage B strain) and TIV-YB (with respect to the *Victoria* lineage B strain) after completion of the vaccination series in children 3 to 17 years of age.
- The study also achieved its confirmatory secondary objective of demonstrating that, in children 3 to 17 years of age, the immunogenic response to the alternate, Yamagata-lineage, B strain in FLU Q-QIV fulfilled CBER's immunogenicity criteria predictive of clinical benefit.
- The descriptive immunogenicity data indicated that, in children 6 to 35 months of age, each of the four strains in the FLU Q-QIV vaccine met CBER's SPR and SCR criteria indicative of clinical benefit with the exception of the SPR for the A/Victoria/210/2009 (H3N2) strain.

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Overall Conclusions: (continued):

- Within the 7 day post-vaccination period, 77.3 %, 71.6% and 69.0% of subjects in the QIV1, TIV-VB, and TIV-YB groups (3-17 years of age), respectively, and 74.8% of subjects in the QIV2 group (6-35 months of age) reported at least one solicited or unsolicited adverse event AE).

- Within the 28 day post-vaccination period, 30.4% , 31.3%, and 29.5% of subjects in the QIV1, TIV-VB, and TIV-YB groups (3-17 years of age), respectively, and 53.2% of subjects in the QIV2 group (6-35months of age) reported at least one unsolicited adverse event.

- Within the entire study period, 37.1%, 36.1%, and 37.6% of subjects in the QIV1, TIV-VB, and TIV-YB groups (3-17 years of age), respectively, and 48.8% of subjects in the QIV2 group (6-35months of age) reported at least one medically-attended adverse event (MAE).

- No fatal serious adverse events (SAEs) were reported during the entire study period.

- Two SAEs (angioedema and conjunctivitis), reported for one subject in the TIV-YB group (3-17 years of age), were considered by the investigator to be related to the vaccination. Both SAEs were reported to have recovered/resolved.

- Two SAEs (grand mal convulsion in PID (b) (6) with onset on the day of the first dose of Q-QIV and febrile convulsion in PID (b) (6) with onset on 18 days after first dose of Q-QIV) reported in the QIV2 group (6-35 months of age) were considered by investigator to be related to the vaccination. Both SAEs were reported to have recovered/resolved.

Date of report: Amendment 1 Final: 28 June 2012

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MODULAR APPENDICES

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LIST OF ABBREVIATIONS

°C	Degrees Celsius
°F	Degrees Fahrenheit
µg	microgram
ACIP	Advisory Committee on Immunization Practices
AE	Adverse event
ATP	According to protocol
eCRF	electronic Case Report Form
DIL	Dilution
FDA	Food and Drug Administration, United States
F/U	Follow-up
GCP	Good Clinical Practice
GMT	Geometric Mean Titer
GSK	GlaxoSmithKline
GSM	Global Study Manager
HA	Haemagglutinin
HI	Haemagglutinin inhibition
H1N1v	H1N1 variant
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IM	Intramuscular
IND	Investigational New Drug
IRB	Institutional Review Board

IUD	Intrauterine device
LAR	Legally Acceptable Representative
LSC	Local Study Contact
MAE	Medically attended adverse event
MedDRA	Medical Dictionary for Regulatory Activities
mL	Milliliter
Mm	Millimeter
pIMD	Potential Immune-Mediated Disease
Q	Quebec (manufactured in)
QIV	Quadrivalent Influenza Vaccine
RDE	Remote data entry
SAE	Serious Adverse Event
SBIR	Simply the Best Internet Randomization
SCF	Seroconversion factor
SCR	Seroconversion rate
SPC	Summary of product characteristics
SPM	Study Procedures Manual
SPR	Seroprotection rate
TF	Thimerosal-free
TIV	Trivalent Influenza Vaccine
TVC	Total vaccinated cohort
USPHS	US Public Health Service

GLOSSARY OF TERMS

Adequate contraception: Adequate contraception is defined as a contraceptive method with failure rate of less than 1% per year when used consistently and correctly (when applicable, as mentioned in the product label) for example abstinence, combined or progestogen oral contraceptives, injectable progestogen, implants of levonorgestrel, oestrogenic vaginal ring, percutaneous contraceptive patches or intrauterine device (IUD) or intrauterine system (IUS), vasectomy with documented azoospermia of the sole male partner or double barrier method (condom or occlusive cap plus spermicidal agent).

For azoospermia, 'documented' refers to the laboratory report of azoospermia, required for acceptable documentation of successful vasectomy in the subject's male partner.

Adverse event: Any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.

Blinding: A procedure in which one or more parties to the trial are kept unaware of the treatment assignment in order to reduce the risk of biased study outcomes. In an observer-blind study, the subject and the site and sponsor personnel involved in the clinical evaluation of the subjects are blinded while other study personnel may be aware of the treatment allocation (see Section 5.4.4 for details on observer-blinded studies). The level of blinding is maintained throughout the conduct of the trial, and only when the data are cleaned to an acceptable level of quality will appropriate personnel be unblinded or when required in case of a serious adverse event.

Child in care A child who has been placed under the control or protection of an agency, organisation, institution or entity by the courts, the government or a government body,

	acting in accordance with powers conferred on them by law or regulation. The definition of a child in care can include a child cared for by foster parents or living in a care home or institution, provided that the arrangement falls within the definition above. The definition of a child in care does not include a child who is adopted or has an appointed legal guardian.
Completed:	Subjects who completed the last study visit.
Diary card:	Cards given to the parents /guardians /subjects by the investigator to record adverse events following vaccination.
Eligible:	Qualified for enrolment into the study based upon strict adherence to inclusion/exclusion criteria.
Epoch:	An epoch is a well defined part of a protocol that covers a set of consecutive time-points. Generally, an epoch is self-contained and allows one to perform a data analysis to address some of the trial objectives (e.g. primary, booster, yearly follow-ups,…).
eTrack:	GSK's tracking tool for clinical trials.
Evaluable:	Meeting all eligibility criteria, complying with the procedures defined in the protocol, and, therefore, included in the according-to-protocol (ATP) analysis.
Geometric Mean Titer (GMT)	The anti-log of the mean of the log (base 10) transformed inverse titers (the number X would denote the inverse of a titer expressed as "1:X"). Antibody titers below the cut-off of the assay are given an arbitrary value of half the cut-off for the purpose of GMT calculation.
Global Study Manager	An individual assigned by GSK Biologicals Headquarters who is responsible for assuring the co-ordination of the operational aspects and proper conduct of a clinical study, including compliance with International Conference on Harmonisation (ICH) Harmonised Tripartite Guideline for Good Clinical Practice (GCP) and GSK policies and standard operating procedures.
Investigational vaccine/product: **(Synonym of Investigational Medicinal**	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used in a way different from the approved form, or when used for an unapproved indication, or when used to gain

Product)	further information about an approved use.
Medical Monitor:	An individual medically qualified to assume the responsibilities of the sponsor (GSK Biologicals) especially in regards to the ethics, clinical safety of a study and the assessment of adverse events.
Medically Attended Adverse Event	An event for which the subject received medical attention defined as hospitalization, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason
Menarche:	Menarche is the onset of menses for the first time in a young female and is preceded by several changes associated with puberty including breast development and pubic hair growth. Menarche usually occurs within 1-2 years of breast development, thelarche. However, a young female can become pregnant before her first menses. Thus, a conservative definition of non-childbearing potential in a pre-menarcheal female is a young female who has not yet entered puberty as evidenced by lack of breast development (palpable glandular breast tissue).
Primed subjects	All subjects ≥ 9 years of age and any subjects aged 6 months to 8 years who have received at least one dose of an influenza A (H1N1) 2009 monovalent vaccine in the last season (or had laboratory confirmed H1N1 infection) AND have received two doses of seasonal influenza vaccine separated by at least one month during the last season or have received at least one dose prior to last season.
Protocol amendment:	ICH defines a protocol amendment as: 'A written description of a change(s) to or formal clarification of a protocol.' GSK Biologicals further details this to include a change to an approved protocol that affects the safety of subjects, scope of the investigation, study design, or scientific integrity of the study.
Protocol administrative change:	A protocol administrative change addresses changes to only logistical or administrative aspects of the study. NB Any change that falls under the definition of a protocol amendment (e.g. a change that affects the safety of subjects, scope of the investigation, study design, or scientific integrity of the study) MUST be prepared as an amendment to the protocol.

Randomization:	Process of random attribution of treatment to subjects in order to reduce bias of selection
Serious adverse event:	Any untoward medical occurrence in a patient or clinical investigation subject that: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.
Seroconversion Factor (SCF)	SCF is defined as the fold increase in serum HI GMTs post-vaccination compared to Day 0 (i.e., the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the pre-vaccination reciprocal HI titer).
Seroconversion Rate (SCR)	SCR is defined as the proportion of vaccinees who have either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least a four-fold increase in post-vaccination titer.
Seroprotection Rate (SPR)	The seroprotection rate or SPR is defined as the proportion of vaccinees with a serum HI titer ≥ 1:40
Site Monitor:	An individual assigned by the sponsor who is responsible for assuring proper conduct of clinical studies at one or more investigational sites.
Solicited adverse event:	Adverse events (AEs) to be recorded as endpoints in the clinical study. The presence/occurrence/intensity of these events is actively solicited from the subject or an observer during a specified post-vaccination follow-up period.
Subject:	Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the clinical study, either as a recipient of the product(s) or as a control.
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the study.
Treatment:	Term used throughout the clinical study to denote a set of investigational product(s) or marketed product(s) or placebo intended to be administered to a subject, identified by a unique number, according to the study randomisation or treatment allocation.
Treatment number:	A number identifying a treatment to a subject, according to the study randomisation or treatment allocation.

Unprimed subjects	Subjects aged 6 months to 8 years who have not received any influenza A (H1N1) 2009 monovalent vaccine in the last season (or did not have laboratory confirmed H1N1 infection) OR who have not received any seasonal influenza vaccine in the past or received only one dose for the first time in the last influenza season.
Unsolicited adverse event:	Any adverse event (AE) reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited adverse event.

TRADEMARKS

The following trademarks are used in the present report.

Note: In the body of the Study Report (including the synopsis), the names of the vaccines and/or medications will be written without the subscript symbol ™ or ®.

Trademarks of the GlaxoSmithKline group of companies	generic description
Fluarix®	Trivalent inactivated influenza vaccine

1. ETHICS

1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, any amendments, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational center IRB.

1.2. Ethical conduct of the study

This study was conducted in accordance with "good clinical practice" (GCP) and all applicable regulatory requirements, including, where applicable, the Declaration of Helsinki.

1.3. Subject information and consent

Written informed consent was obtained from each pediatric subject's parent(s)/Legally Acceptable Representative (LAR) prior to the performance of any study-specific procedures. Case report forms were provided for each subject's data to be recorded.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

2.1. Administrative structure

This study was conducted by 32 principal investigators at 32 centers across Canada, Mexico, Spain, Taiwan, and the United States.

The Sponsor (GSK Biologicals) was responsible for administration of the study including clinical trial supply management and laboratory facilities.

2.2. Clinical Study Report revision history

An error was observed in the approved original report dated 01 December 2011. A single page which contained Section 8.5 ('adverse events leading to premature discontinuation of study vaccine and/or study') and Section 8.6 ('other significant adverse events') and was present in the final approved draft, but which was inadvertently omitted from the final published report. This amendment to the report restores the missing Sections, including Sub-section 8.6.1 (potential immune-mediated diseases).

3. INTRODUCTION

Influenza is a serious public health problem. The influenza virus is an important respiratory pathogen that causes annual epidemics and occasional pandemics. Every year, various strains of influenza virus circulate throughout the world, often causing outbreaks and epidemics. Epidemics occur almost exclusively in the 'winter' months in the Northern Hemisphere (October to April) and in May to September in the Southern

Hemisphere. Virtually every year, epidemic influenza has a significant impact in terms of morbidity, mortality, and economic burden. Influenza affects 5 to 15% of the population in all age groups [Nicholson, 2003]. This figure may rise to 30% during major epidemics, leading to the disruption of many activities in the community and overloading health care systems. The World Health Organization (WHO) estimates that annual epidemics of influenza cause three to five million cases of severe illness and 250,000 to 500,000 deaths. For example, in the United States alone, influenza is responsible for substantial morbidity and mortality, with an average of over 226,000 excess hospitalizations [Thompson, 2004] and approximately 36,000 deaths annually [Thompson, 2003].

Influenza disease is caused by a viral infection of the respiratory tract from which people may suffer repeatedly during their lives. Influenza is transmitted from person to person mainly through aerosol sprays of infectious respiratory secretions caused by coughing and sneezing, or by direct contact with an infected person. Rates of infection are highest among children. The highest influenza burden in terms of pediatric respiratory admissions is seen in infants 6 to 11 months of age [Schanzer, 2006] and rates of illness in children younger than 2 years of age are substantially higher than those in children 2 years of age or older [Poehling, 2006]. Children also play an important role in the spread of the disease [Brownstein, 2008], possibly because of their sustained high levels of virus shedding. Since annual influenza vaccination is currently the most effective means of controlling influenza and preventing its complications and mortality [WHO, 2009], there is a general trend to extend the recommendation for influenza vaccinations not only to infants with high risk of complications, but also to healthy children and adolescents. The Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control (CDC) has recommended seasonal influenza vaccination for all persons aged 6 months and older [ACIP, 2010]. The effectiveness of influenza vaccination is, however, dependent on adequate matching between the circulating viruses and the viruses contained in the vaccine.

Since 1983, two antigenically distinct lineages of influenza B have circulated in the world. Their co-existence has also resulted in the emergence and subsequent worldwide circulation of a reassortant B virus possessing a Victoria-lineage hemagglutinin (HA) with a Yamagata-lineage derived neuraminidase [Barr, 2003]. In the United States, both Yamagata and Victoria lineages have co-circulated since the 2001-2002 influenza season.

From 2001 to 2009, influenza B viruses have accounted for 6.9% to 38.7% of clinical isolates from CDC surveillance [CDC, 2010]. In 5 of these 8 years, a substantial proportion of B virus isolates have been representative of the genetic lineage not included in the trivalent vaccine, and have accounted for 6.4% to 29.9% (median of 8.5%) of all influenza virus isolates [CDC, 2010].

The consequences of such a B virus mismatch could be severe. During the 2007-2008 season, almost 30% of influenza viruses tested at the CDC in the United States were type B, and 98% of them did not match the lineage contained in the trivalent vaccine [CDC, 2008]. Assuming that a quadrivalent vaccine containing a second B strain had been used in the 2007-2008 season rather than a trivalent vaccine, a public health impact model for influenza-associated health outcomes estimated that the quadrivalent seasonal vaccine

could have prevented an additional 1,090,514 influenza cases, and resulted in 7,488 fewer hospitalizations and 321 fewer deaths [Reed, 2009]. Since the two evolutionarily distinct lineages of influenza B virus continue to co-circulate, and because cross-reactivity between the two lineages is low in the pediatric population (which has limited immunologic experience with influenza), an additional B strain antigen in the seasonal vaccine may offer greater efficacy and broader protection to children (Englund, 2006; Levandowski, 1991). In addition, the 2007-8 experience suggested that mismatched B virus morbidity was substantial in the elderly [Proff, 2009]; and these vulnerable persons could benefit from improved herd immunity in children as well as direct immunization. These considerations have lead GSK Biologicals to develop a candidate quadrivalent seasonal influenza vaccine, FLU Q-QIV (GSK2282512A), comprised of two A and two B strains.

Fluarix-VB (Victoria lineage B strain) and *Fluarix*-YB (Yamagata lineage B strain) are two of GSK Biologicals' licensed trivalent vaccines (TIV) formulated with the same two influenza A strains (A/H1N1 and A/H3N2), but with different B strains. *Fluarix*-VB is identical to *Fluarix* and *Fluarix*-YB contains an alternate Yamagata lineage B strain, but otherwise is also identical to *Fluarix*.

The purpose of this study was to assess, in subjects 3 to 17 years old, non-inferiority of the quadrivalent FLU Q-QIV vaccine compared to trivalent *Fluarix*-VB (TIV-VB), and *Fluarix*-YB (TIV-YB) with respect to the immunogenicity of the shared virus strains and immunological superiority of FLU Q-QIV compared to *Fluarix*-VB with respect to the Yamagata B lineage strain and to *Fluarix*-YB with respect to the Victoria B lineage strain. The study design relied on FDA/CBER guidance on statistical criteria for immunological endpoints and recommendation for comparison to a US-licensed seasonal inactivated influenza vaccine [FDA, 2007] to infer immunogenic non-inferiority. In addition, a descriptive evaluation of the safety and immunogenicity of FLU Q-QIV was made in younger children (6 to 35 months old) in a separate and independent arm of the study.

Fluarix is a US-licensed seasonal inactivated influenza vaccine. Given that serum HI antibody titers are generally considered to be a marker of protective immunity, a demonstration of immunogenic non-inferiority by HI assay to *Fluarix* would, therefore, provide evidence of FLU Q-QIV effectiveness in children 3 to 17 years of age. In addition, a tolerability and safety profile similar to *Fluarix* would indicate acceptability comparable to an existing licensed product.

4. STUDY OBJECTIVES

See Section 5.10 for details of the study endpoints.

4.1. Primary objectives

- To test the immunogenic non-inferiority (in terms of *Geometric Mean Titer [GMT] and *Seroconversion Rate [SCR]), for the shared viral strains of FLU Q-QIV versus *Fluarix*-VB and *Fluarix*-YB in children 3 to 17 years old approximately 28 days after completion of dosing (approximately at Day 28 for primed subjects and approximately at Day 56 for unprimed subjects).

  Criteria to conclude non-inferiority:

  The test of non-inferiority was based on the analysis of the entire 3 to 17 year-old age range in each treatment group, and immunogenic non-inferiority was concluded if:

  – The upper limit of the two-sided 95% confidence interval of the GMT ratio (*Fluarix* /FLU Q-QIV) after completion of the vaccination series did not exceed 1.5 for the three strains (H3N2, H1N1 and shared B) contained in each *Fluarix* vaccine *and*

  – The upper limit of the two-sided 95% confidence interval for the difference in SCR (Fluarix minus FLU Q-QIV) did not exceed 10% for the three strains contained in each Fluarix vaccine.

- *See glossary for definitions of Geometric Mean Titer and Seroconversion Rate.

4.2. Secondary objectives

- To test the immunogenic superiority of the B strains present in FLU Q-QIV (in terms of *GMT ratio and *SCR) in children 3 to 17 years old approximately 28 days after completion of dosing (approximately at Day 28 for primed subjects; approximately at Day 56 for unprimed subjects) by comparing

  – FLU Q-QIV to *Fluarix*-YB with respect to the Victoria lineage B strain, and

  – FLU Q-QIV to *Fluarix*-VB with respect to the Yamagata lineage B strain

  Criteria to conclude superiority:

  The test of immunogenic superiority was based on the analysis of the entire 3 to 17 year-old age range in each treatment group, and immunogenic superiority was concluded if the lower limit of the two-sided 95% confidence interval on *GMT ratio (FLU Q-QIV over Fluarix) was greater than 1.5 and the difference in *SCR (FLU-Q-QIV minus Fluarix) was greater than 10%.

  *See glossary for definitions of GMT and SCR.

- To describe the immunogenicity (in terms of *Geometric Mean Titer [GMT], *seroprotection rate [SPR], *seroconversion rate [SCR] and *seroconversion factor [SCF]) of FLU Q-QIV and each *Fluarix* vaccine overall and for the age categories 3 to 8 years and 9 to 17 years, and of FLU-Q-QIV for the 6-35 months age group

- To evaluate fulfilment of CBER immunogenicity criteria by the immune response to the alternate, Yamagata lineage, B strain in FLU Q-QIV (in 3-17 year olds)

  (CBER criteria [FDA, 2007] are met if the lower limit of 95% CI for SCR is ≥40% and post-vaccination SPR is ≥70%)

  *See glossary for definitions of GMT, SPR, SCR, and SCF.

- To evaluate and describe the reactogenicity and safety of FLU Q-QIV and each *Fluarix* vaccine overall in the 3 to 17 years age category and for the age categories 3 to 8 years and 9 to 17 years. The reactogenicity and safety of FLU-Q-QIV for the 6-35 month age group were also described. The following reactogenicity and safety analyses were performed:

  – Solicited local symptoms during the 7-day post-vaccination follow-up (day of vaccination and 6 subsequent days) overall (3-17 years) and in three age groups (6 to 35 months, 3-8 years, 9-17 years).

  – Solicited general symptoms during the 7-day post-vaccination follow-up (day of vaccination and 6 subsequent days) overall (3-17 years), and for the 6 to 35 months, 3 to 4 year, 5 to 8 year and 9 to 17 year old age groups (note that the 3-4 year-old and 5-8 year old groups were assessed using different solicited general symptoms because of their differential reporting abilities, and were thus analyzed separately for this category).

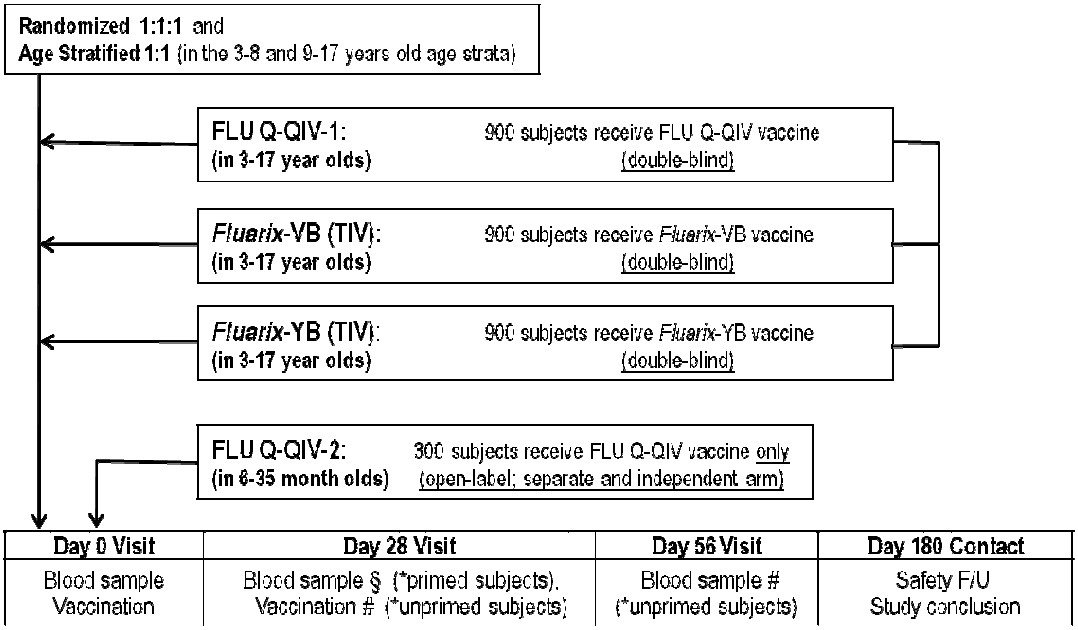
  – Unsolicited symptoms during the 28-day (day of vaccination and 27 subsequent days) post-vaccination follow-up period overall (3-17 years) and in the 6 to 35 month, 3-8 years and 9-17 years age groups.

  – Serious adverse events (SAEs), medically-attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period (Day 0 to Day 180 after the first vaccination), overall (3-17 years) and in the 6 to 35 months, 3-8 years and 9-17 years age groups.

5. INVESTIGATIONAL PLAN

5.1. Study design

5.1.1. Overall study design – Description



F*luarix*-VB = *Fluarix* TIV-VB (Victoria lineage B strain)
Fluarix-YB = *Fluarix* TIV-YB (Yamagata lineage B strain)
FLU Q-QIV-1 group = FLU Q-QIV administered to 3-17 year old subjects
FLU Q-QIV-2 group = FLU Q-QIV administered to 6-35 month old subjects; no analytical comparisons to TIV groups
* Refer to glossary for definitions of primed and unprimed subjects;
§ For primed subjects only # For unprimed subjects only

Experimental design: Phase III, double-blind, randomized, controlled, parallel-group, multi-center, and multi-country study

Treatment allocation: Subjects will be randomized 1:1:1 in the FLU Q-QIV, *Fluarix*-VB, and *Fluarix*-YB groups and age stratified 1:1 into the 3-8 years and 9-17 years age strata. The contrast between FLU Q-QIV and each *Fluarix* vaccine will be double-blind and limited to the 3 to 17 year-old stratum and there will be a separate and independent open-label arm to evaluate FLU Q-QIV in the 6 to 35 months old age stratum:

- For the FLU Q-QIV and each *Fluarix* contrast, age (3 to 4 years and 5 to 8 years old), country, and the pre-study influenza priming status of subjects < 9 years old will be treated as minimization factors to ensure equal representation of younger vs. older (in the 3-8 years age strata) and of primed vs. unprimed subjects in the two treatment groups.

Blinding: Double-blind for the comparison of FLU Q-QIV to each *Fluarix* vaccine in 3 to 17 year old subjects and open-label for the descriptive evaluation of FLU Q-QIV in 6 to 35 month old subjects. Since the separate, open-label, FLU Q-QIV only group is an independent and stand alone arm with no contribution to the primary study objectives and

there are no analytical plans to include data from the open-label arm (6 to 35 month old subjects) with the analysis of data from the other three blinded arms (3 to 17 year old subjects), the blinding for this study is effectively considered to be double-blind.

Treatment groups: *Planned* number of subjects per group

- Q-QIV-1 (FLU Q-QIV): 900 subjects (3 to 17 years old)
- TIV-VB (*Fluarix*-VB): 900 subjects (3 to 17 years old)
- TIV-YB (*Fluarix*-YB): 900 subjects (3 to 17 years old)
- Q-QIV-2 (FLU Q-QIV): 300 subjects (6 to 35 months old)

Vaccination schedule for subjects 6 months to 8 years of age:

- One intramuscular (IM) injection at Day 0 for *primed subjects
- Two IM injections (one each at Day 0 and at Day 28 for *unprimed subjects)

  *see glossary for definitions of primed and unprimed subjects

Vaccination schedule for subjects 9 to 17 years of age:

- One IM injection at Day 0.

Immunogenicity (blood) sampling: Blood samples collected at Day 0 and 28 days for primed subjects and at Day 0 and Day 56 for unprimed subjects.

Control: Active comparators (*Fluarix*-VB and *Fluarix*-YB).

Type of study: Self-contained.

Data collection: Remote Data Entry (RDE) - electronic Case Report Form (eCRF).

Duration of the study: It was expected that all subjects would be enrolled within approximately 4 to 8 weeks. The study duration was to be approximately 6 months for all subjects.

Serious adverse events (SAEs) and medically attended adverse events (MAEs): SAEs and MAEs were to be reported in a prospective manner throughout the study period, i.e. the period beginning with administration of the first vaccine dose (at Day 0) and ending at Day 180 for all subjects.

Study Visits: For primed subjects, there were 2 scheduled visits: on Day 0 (Visit 1-Blood sample and vaccination) and Day 28 (Visit 2-Blood sample and conclusion of active phase). For unprimed subjects, there were 3 scheduled visits: on Day 0 (Visit 1-Blood sample and vaccination), on Day 28 (Visit 2-Vaccination), and on Day 56 (Visit 3-Blood sample and conclusion of active phase). On Day 180 there was a contact for safety follow-up and for study conclusion for all study subjects.

5.1.2. Discussion of study design

The purpose of this study was to assess, in subjects 3 to 17 years old, non-inferiority of the quadrivalent FLU Q-QIV vaccine compared to trivalent *Fluarix*-VB (TIV-VB), and *Fluarix*-YB (TIV-YB) with respect to the immunogenicity of the shared virus strains and immunological superiority of FLU Q-QIV compared to *Fluarix*-VB with respect to the Yamagata B lineage strain and to *Fluarix*-YB with respect to the Victoria B lineage strain. In addition, a descriptive evaluation of the safety and immunogenicity of FLU Q-QIV was made in younger children (6 to 35 months old) in a separate and independent arm of the study.

Fluarix is a US-licensed seasonal inactivated influenza vaccine. Given that serum HI antibody titers are generally considered to be a marker of protective immunity, a demonstration of immunogenic non-inferiority by HI assay to *Fluarix* would, therefore, provide evidence of FLU Q-QIV effectiveness in children 3 to 17 years of age. In addition, a tolerability and safety profile similar to *Fluarix* would indicate acceptability comparable to an existing licensed product.

Fluarix-VB (Victoria lineage B strain) and *Fluarix*-YB (Yamagata lineage B strain) are GSK Biologicals' licensed trivalent vaccines formulated with the same two influenza A strains (A/H1N1 and A/H3N2), but with different B strains. *Fluarix*-VB was identical to *Fluarix* and *Fluarix*-YB contained an alternate Yamagata lineage B strain, but otherwise was also identical to *Fluarix*. The Victoria lineage B strain in *Fluarix*-VB was the B strain recommended by the WHO for the Northern Hemisphere 2010-2011 influenza season, while the Yamagata lineage B strain in *Fluarix*-YB was not included in the 2010-2011 season recommendation. The quadrivalent FLU Q-QIV vaccine was formulated with two influenza A strains (A/H1N1 and A/H3N2) and two influenza B strains (the same Victoria lineage B strain as that in *Fluarix*-VB, as well as a second, Yamagata lineage, B strain). All vaccine formulations proposed to be used in this study were free of thimerosal (also known as thiomersal).

The study featured a double-blind, parallel group, design with a 1:1:1 randomization between FLU Q-QIV, *Fluarix*-VB, and *Fluarix*-YB (900 subjects each; 3 to 17 years old) to provide optimum power for the non-inferiority and superiority contrasts and, separately in an independent stand alone arm, administration of open-label FLU Q-QIV to 300 subjects, 6 to 35 months old. Randomization was stratified by age, because both increasing immunologic maturity and also because prior lifetime exposure to either influenza vaccine or influenza virus is known to provide immunologic priming.

This parallel group design allowed a comparison of the safety and immunogenicity of the quadrivalent FLU Q-QIV vaccine to the trivalent (TIV) *Fluarix* vaccines in children 3 years and older with optimum power to demonstrate non-inferior immunogenicity of the common strains in the QIV and TIV vaccines and immunological superiority of FLU Q-QIV compared to *Fluarix*-VB with respect to the Yamagata lineage B strain and to *Fluarix*-YB with respect to the Victoria lineage B strain. In addition, a descriptive evaluation of the safety and immunogenicity of FLU Q-QIV was made in younger children (6 to 35 months old) in a separate and independent arm of the study. These data are expected to provide the basis for future comparison of FLU Q-QIV immunogenicity

in North American children with that observed in children of the same age in a planned comparator (irrelevant)-controlled efficacy trial, which cannot be conducted in North America due to pre-existing influenza vaccine recommendations for this age group throughout Canada, the US, and Mexico.

Immunological non-inferiority was assessed in terms of the humoral immune response (GMT ratio and SCR), of the FLU Q-QIV vaccine compared to the response of the *Fluarix* TIV vaccines with respect to the shared virus strains. Immunological superiority was assessed in terms of the humoral immune response (GMT ratio and SCR) of the FLU Q-QIV vaccine compared to the response of *Fluarix*-VB and *Fluarix*-YB with respect to the Yamagata B and Victoria B strains, respectively. Immune responses in terms of GMT, SCR, SPR, and SCF (see glossary for definitions) were described for all strains in all subjects, including the 3-8 and 9-17 years age groups.

Subjects for the FLU-Q-QIV and *Fluarix* comparisons were stratified based on two age groups: 3 to 8 years old, and 9 to 17 years of age, because both increasing immunologic maturity and also because prior lifetime exposure to either influenza vaccine or influenza virus is known to provide immunologic priming. Within each age stratum, subject randomization for vaccine administration was in a 1:1 ratio with respect to Flu-Q-QIV and each *Fluarix* (VB or YB). Prior vaccine priming status (please refer to the glossary for definitions of unprimed and primed subjects), country, and the age sub-segments of 3 to 4 years and 5 to 8 years were considered as minimization factors. There was no age stratification in the 6 to 35 months old age group in the separate and independent, open-label, FLU Q-QIV only arm of the study.

Two 0.5 mL doses of FLU Q-QIV or *Fluarix* were administered intramuscularly at an approximate 28 days interval to children 3 to 8 years old who were unprimed, as is standard practice for all inactivated influenza vaccines given to this age group in most countries e.g., in the US, Canada, Mexico, and in European countries. Primed subjects 3 to 8 years old and all subjects 9 to 17 years old (all considered to be primed) received a single 0.5 mL dose consistent with current recommendations for standard TIV.

For the 6 to 35months old subjects in the open-label arm of the study, two 0.5 mL doses of FLU Q-QIV were administered intramuscularly at an approximate 28 days interval to unprimed subjects. Primed subjects in this age group received a single 0.5 mL dose of FLU Q-QIV in line with current recommendations for standard TIV.

A double-blind design for the non-inferiority and superiority contrasts protected study endpoints from bias.

5.2. Study procedures

5.2.1. Outline of study procedures

Study procedures are outlined in Table 1 for unprimed subjects and Table 2 for primed subjects.

Table 1 Outline of study procedures for unprimed subjects receiving 2 doses of vaccine

Age (m = months; y = years)	[6m to 17y]	[7m to 17y 1m]	[8m to 17y 2m]	[12m to 17y 6m]
Epoch	***Primary***			
Type of contact	**Visit 1**	**Visit 2**	**Visit 3**	**Visit/Phone**
Timepoints	**Day 0**	**Day 28**	**Day 56**	**Day 180***
Sampling time points	**Pre-vacc**	**Post-vacc 1**	**Post-vacc 2**	**ESFU**
Informed consent by parent(s)/Legally Acceptable representative(s) (LAR)	●			
Informed assent where appropriate	○			
Check inclusion/exclusion criteria	●			
Check elimination criteria		●	●	●
Check contraindications to vaccination	●	●		
Collect demographic data	●			
Medical history	●			
History of influenza vaccination	●			
Physical examination(history directed)	●	○§	○§	
Pre-vaccination body temperature	●	●		
Urine pregnancy test for girls of child-bearing potential	●	●		
Internet randomization	●			
Blood sampling (approximately 4 ml) for humoral immune response determination	●		●	
Vaccination	●	●		
Distribution of diary cards for post-vaccination recording of solicited symptoms daily** (Days 0-6) and unsolicited symptoms (Days 0- 27)	○	○		
Return of diary cards		○	○	
Diary card transcription by investigator		●	●	
Record any concomitant medication/vaccination	●	●	●	●
Record any intercurrent medical condition	●	●	●	●
Query/Reporting of MAEs, SAEs, and pIMDs	●ϕ	●	●	●
Ask parent(s)/LAR(s) if he/she may be contacted regarding subject's possible future study participation				●
Study conclusion			●‡	●

● Vacc: vaccination. ESFU: Extended safety follow-up.

● is used to indicate a study procedure that required documentation in the individual CRF

○ is used to indicate a study procedure that did not require documentation in the individual CRF

* Day 180 from first vaccination

** Parent(s)/LAR(s) were instructed to immediately report any convulsion (seizure) or fever ≥39˚C (102.2˚F) occurring in a subject <5 year old within 2 days of vaccination (i.e., day of vaccination and following day)

§ if deemed necessary by the investigator

‡ Conclusion of the vaccination (active) phase

ϕ Prior to vaccination, reporting was limited to Fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

Table 2 Outline of study procedures for primed subjects receiving 1 dose of vaccine

Age (m = months; y = years)	[6m to 17y]	[7m to 17y 1m]	[12m to 17y 6m]
Epoch	***Primary***		
Type of contact	**Visit 1**	**Visit 2**	**Visit/Phone**
Timepoints	**Day 0**	**Day 28**	**Day 180***
Sampling time points	**Pre-vacc**	**Post-vacc 1**	**ESFU**
Informed consent by subject or parent (s)/ Legally Acceptable representative (s) (LAR) as appropriate	•		
Informed assent where appropriate	○		
Check inclusion/exclusion criteria	•		
Check elimination criteria		•	•
Check contraindications to vaccination	•		
Collect demographic data	•		
Medical history	•		
History of influenza vaccination	•		
Physical examination (history directed)	•	○§	
Pre-vaccination body temperature	•		
Urine pregnancy test for girls of child-bearing potential	•		
Internet randomization	•		
Blood sampling (approximately 4 ml) for humoral immune response determination	•	•	
Vaccination	•		
Distribution of diary cards for post-vaccination recording of solicited symptoms daily** (Days 0-6) and unsolicited symptoms (Days 0-27)	○		
Return of diary cards		○	
Diary card transcription by investigator		•	
Record any concomitant medication/vaccination	•	•	•
Record any intercurrent medical condition	•	•	•
Query/Reporting of MAEs, SAEs, and pIMDs	•ϕ	•	•
Ask parent(s)/LAR(s) if he/she may be contacted regarding subject's possible future study participation			•
Study conclusion		•‡	•

Vacc: vaccination. ESFU: Extended safety follow-up.

• is used to indicate a study procedure that required documentation in the individual CRF

○ is used to indicate a study procedure that did not require documentation in the individual CRF

* Day 180 from first vaccination

** Parent(s)/LAR(s) were instructed to immediately report any convulsion (seizure) or fever ≥39˚C (102.2˚F) occurring in a subject <5 year old within 2 days of vaccination (i.e., day of vaccination and following day)

§ if deemed necessary by the investigator

‡ Conclusion of the vaccination (active) phase

ϕ Prior to vaccination, reporting was limited to Fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

5.2.2. Intervals between study visits

The intervals between the study visits are shown in Table 3 (primed subjects) and in Table 4 (unprimed subjects). Data obtained from subjects were not eligible for inclusion in the according-to-protocol (ATP) analysis if the study visit was made outside the indicated intervals.

Table 3 Intervals between study visits – primed subjects

Interval	Minimum and maximum interval allowed †
1 (Day 0 Visit → Day 28 Visit)	25-42 days
2 (Day 0 Visit → Day 180 Safety follow-up)	166-201 days

†. Subjects will not be eligible for inclusion in the ATP immunogenicity cohort analysis if they make the study visit outside this interval. Whenever possible, the investigator should arrange study visits within this interval.

Table 4 Intervals between study visits – unprimed subjects

Interval	Minimum and maximum interval allowed †
1 (Visit 1, Day 0→Visit 2, Day 28)	25-42 days
2 (Visit 2 Day 28→Visit 3 Day 56)	25-42 days
3 (Visit 1, Day 0 → Safety follow-up Day 180)	166-201 days

†. Subjects will not be eligible for inclusion in the ATP immunogenicity cohort r analysis if they make the study visit outside this interval. Whenever possible, the investigator should arrange study visits within this interval.

5.3. Selection of study population

This was a multicenter study conducted in Canada, Mexico, Spain, Taiwan, and the United States. The target number of subjects was approximately 2700 male and female children aged 3 to 17 years old (900 subjects randomly assigned to each of three groups, FLU Q-QIV, *Fluarix*-VB, and *Fluarix*-YB). An additional 300 eligible subjects, 6 to 35 months old, were enrolled in a separate and independent, open-label, FLU Q-QIV only arm of the study.

5.3.1. Inclusion criteria

All subjects were required to satisfy ALL of the following criteria at study entry:

- Subjects and/or subjects' parent(s)/Legally Acceptable Representative(s) (LAR) who the investigator believed could and would comply with the requirements of the protocol (e.g. completion of the diary cards, return for follow-up visits, respecting intervals between study visits).
- A male or female child aged between 6 months and 17 years of age inclusive (i.e., had not yet attained their 18th birthday) at the time of the first vaccination; children were eligible regardless of history of administration of influenza vaccine in a previous season.
- Written informed consent obtained from the subject/from the parent(s)/LAR(s) of the subject.
- Subjects in stable health as determined by investigator's clinical examination and assessment of subjects' medical history.
- Female subjects of non-childbearing potential could be enrolled in the study.

  Non-childbearing potential was defined as pre-menarche, current tubal ligation, hysterectomy, or ovariectomy. Please refer to the Glossary of Terms for the definition of menarche.

- Female subjects of childbearing potential could be enrolled in the study, if the subject:
  - had practiced adequate contraception for 30 days prior to vaccination, and
  - had a negative pregnancy test on the day of vaccination, and
  - had agreed to continue adequate contraception during the entire treatment period and for 2 months after completion of the vaccination series.

Please refer to the Glossary of Terms for the definition of adequate contraception.

5.3.2. Exclusion criteria

The following criteria were checked at the time of study entry. If **ANY** exclusion criterion applied, the subject was not to be included in the study:

- Child in care (please refer to the Glossary of Terms for the definition of child in care.)
- Use of any investigational or non-registered product (drug or vaccine) other than the study vaccines within 30 days preceding the first dose of study vaccine, or planned use during the study period. Routine registered childhood vaccinations were permitted.
- Prior receipt of any seasonal or pandemic influenza vaccine (registered or investigational) within 6 months preceding the first dose of study vaccine, or planned use during the study period.
- Chronic administration (defined as more than 14 days in total) of immunosuppressants or other immune modifying drugs within six months prior to the first vaccine dose. For corticosteroids, this meant a dose equivalent to either > 2 mg/kg of body weight or maximum of 20 mg/day of prednisone or equivalent when administered for > 2 weeks. Inhaled and topical steroids were allowed.
- Administration of immunoglobulins and/or any blood products within the 3 months preceding the first dose of study vaccine or planned administration during the study period.
- History of Guillain-Barré-syndrome within 6 weeks of receipt of prior inactivated influenza virus vaccine.
- Any known or suspected allergy to any constituent of influenza vaccines (including egg proteins); a history of anaphylactic-type reaction to consumption of eggs; or a history of severe adverse reaction to a previous influenza vaccine.
- Fever (temperature ≥ 38.0°C or 100.4°F by any method) at the time of enrolment.
- Acute disease (moderate or severe illness) at the time of enrolment.
- Pregnant or lactating female.
- Female planning to become pregnant or planning to discontinue contraceptive precautions.
- Ongoing aspirin therapy (to avoid potential cases of Reye's syndrome).

- Any confirmed or suspected immunosuppressive or immunodeficient condition, based on medical history and physical examination.
- Any other condition which, in the opinion of the Investigator, prevents the subject from participating in the study.

5.3.3. Elimination criteria

The following criteria were to be checked at each visit subsequent to the first visit. If any became applicable during the study, it did not require withdrawal of the subject from the study but might determine a subject's evaluability in the according-to-protocol (ATP) analysis.

- Use of any investigational or non-registered product (drug or vaccine) other than the study vaccine(s) during the study period. Receipt of routine, registered childhood vaccinations were not elimination criteria.
- Administration of influenza vaccines other than the study vaccines during the active study period.
- Chronic administration (defined as more than 14 days in total) of immunosuppressants or other immune modifying drugs within six months prior to the first vaccine dose. For corticosteroids, this will mean a dose equivalent to either > 2 mg/kg of body weight or > 20 mg/day of prednisone for persons who weigh > 10 kg. Inhaled and topical steroids are allowed.
- Administration of immunoglobulins and/or any blood products during the active study period (i.e., up to the last scheduled blood sampling).
- Condition that had the potential capability of altering the immune response, i.e., any confirmed or suspected immunosuppressive or immunodeficient condition, based on medical history and physical examination.

5.3.4. Contraindications to subsequent doses of vaccine

The following events constituted absolute contraindications to further administration of the study vaccine; if any of these events occurred during the study, the subject was not to receive additional doses of vaccine but could continue other study procedures at the discretion of the investigator. The subject was to be followed until resolution of the event, as with any AE:

- Anaphylaxis following the administration of vaccine(s)

The following events constitute contraindications to administration of the study vaccines at that point in time; if any of these events occur at the time scheduled for vaccination, the subject may be vaccinated at a later date, within the time window specified in the protocol, or withdrawn at the discretion of the investigator:

- Pregnancy
- Fever (temperature ≥ 38.0°C or 100.4°F by any method) at the time of vaccination.
- Acute disease at the time of vaccination. Acute disease was defined as the presence of a moderate or severe illness with or without fever. Study vaccines could be

administered to persons with a minor illness such as diarrhoea, mild upper respiratory infection without fever.

5.3.5. Warnings and precautions

Intramuscular vaccines were to be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding could occur following an intramuscular administration to these subjects. The study vaccines, under no circumstances, were to be administered intravascularly or intradermally.

For additional information, the investigators were referred to the approved product label/package insert for *Fluarix* and to the Investigator Brochure for FLU Q-QIV.

5.3.6. Subject completion and withdrawal from study

5.3.6.1. Subject completion

A subject who returned for the concluding visit foreseen in the protocol was considered to have completed the study.

5.3.6.2. Subject withdrawal from the study

Subjects who were withdrawn because of AEs had to be clearly distinguished from subjects who are withdrawn for other reasons. Investigators were to follow subjects who were withdrawn as result of a SAE/AE until resolution of the event. Subjects who withdrew or were withdrawn from the study were not replaced.

From an analysis perspective, a 'withdrawal' from the study was defined as any subject who did not come back for the concluding visit and/or was not available for the concluding contact foreseen in the protocol.

A subject was considered a 'withdrawal' from the study when no study procedure had occurred, no follow-up had been performed, and no further information had been collected for the subject from the date of withdrawal/last contact. All data collected until the date of withdrawal/last contact of the subject were used for the analysis.

Investigators were to make a reasonable attempt to contact those subjects who did not return for scheduled visits or follow-up.

Information relative to the withdrawal was to be documented in the eCRF. The investigator was to document whether the decision to withdraw a subject from the study was made by the subject himself/herself, by the subject's parent(s) or LAR(s), or by the investigator, as well as which of the following possible reasons was responsible for the withdrawal:

- Serious adverse event
- Non-serious adverse event
- Protocol violation (to be specified by investigator)
- Consent withdrawal, not due to an adverse event

- Moved from the study area
- Lost to follow-up
- Death
- Other (to be specified by investigator)

5.3.6.3. Subject withdrawal from administration of the investigational product

A 'withdrawal' from the investigational product was any subject who did not receive the complete treatment, i.e. when no further planned dose was administered from the date of withdrawal. A subject withdrawn from the investigational product was not necessarily to be withdrawn from the study as further study procedures or follow-up could be performed (safety or immunogenicity) if planned in the study protocol.

Information relative to premature discontinuation of the investigational product was to be documented on the Vaccine Administration screen of the eCRF. The investigator was to document whether the decision to discontinue further vaccination was made by the subject's parent or guardian/LAR or the investigator and which of the following possible reasons was responsible for withdrawal:

- serious adverse event,
- non-serious adverse event,
- other (to be specified by investigator).

5.4. Composition and administration of vaccine(s)

5.4.1. Description of vaccine(s)

All vaccines (*Fluarix*-VB, *Fluarix*-YB, and FLU Q-QIV) to be used in this study have been developed and manufactured by GSK Biologicals and have a thimerosal-free formulation.

Fluarix*-VB (TIV-VB)*:

The trivalent *Fluarix*-VB (Victoria lineage B strain) vaccine was identical to *Fluarix*® and contained HA from three influenza strains, with a total HA content of 45 µg, recommended for the influenza season 2010-2011 by the World Health Organization, CDC/CBER, and EMEA/CHMP:

- H1N1 strain: A/California/7/2009 NYMC X-181 - (15 µg)
- H3N2 strain: A/Victoria/210/2009 NYMC X-187 (an A/Perth/16/2009 [H3N2]-like virus)-(15 µg)
- B strain (Victoria lineage): B/Brisbane/60/2008- (15 µg)

Fluarix*-YB (TIV-YB)*:

Fluarix-YB (Yamagata lineage B strain, but otherwise identical to *Fluarix*®) contained HA from three influenza strains, with a total HA content of 45 µg. The two A strains were identical to those in *Fluarix*-VB above, but the B strain was the most recently

WHO, CDC/CBER, and EMEA/CHMP - recommended B strain from the lineage *not* included in the 2010-2011 WHO recommendations, i.e., Yamagata lineage:

- H1N1 strain: A/California/7/2009 NYMC X-181 - (15 µg)
- H3N2 strain: A/Victoria/210/2009 NYMC X-187 (an A/Perth/16/2009 [H3N2]-like virus)-(15 µg)
- B strain (Yamagata lineage): B/Brisbane/3/2007- (15 µg)

The excipients used in the *Fluarix* formulations complied with the United States and/or European Pharmacopoeia and were as follows: sodium chloride, disodium phosphate dodecahydrate, potassium dihydrogen phosphate, potassium chloride,magnesium chloride hexahydrate, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), octoxynol 10 (Triton X-100), and water for injection.

The commercially available vaccine, *Fluarix*, was assumed to comply with the specifications given in the manufacturer's Summary of Product Characteristics.

FLU Q-QIV:

The FLU Q-QIV vaccine used in the trial had a total HA content of 60 µg.

The quadrivalent FLU Q-QIV vaccine used in the trial had a total HA content of 60 µg. It contained the same influenza A-like and B strains as those described for *Fluarix*-VB above, as well as the most recently WHO, CDC/CBER, and EMEA/CHMP - recommended B strain from the lineage not included in the 2010-2011 WHO recommendations, i.e., B/Florida/4/2006 (15 µg):

- H1N1 strain: A/California/7/2009 NYMC X-179A - (15 µg)
- H3N2 strain: A/Victoria/210/2009 NYMC X-187 (an A/Perth/16/2009 [H3N2]-like virus)-(15 µg)
- B strain (Victoria lineage): B/Brisbane/60/2008- (15 µg)
- B strain (Yamagata lineage): B/Florida/4/2006- (15 µg)

The excipients used in the FLU Q-QIV formulation complied with the United States and/or European Pharmacopoeia and were as follows: sodium chloride, potassium chloride, sodium phosphate dibasic heptahydrate, potassium phosphate monobasic, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80) and water for injection.

Both the *Fluarix* and FLU Q-QIV vaccines are translucent to off-white/grayish opalescent suspensions that may sediment slightly and will be presented in prefilled syringes containing one 0.5 mL dose of vaccine.

The vaccines were labeled and packed according to applicable regulatory requirements.

5.4.2. Dosage and administration

A single recommended dose of either FLU Q-QIV or *Fluarix* (VB or YB) consisted of 0.5 mL vaccine (45 µg HA). The details of vaccine administration are given in Table 5.

Table 5 Vaccine administration

Visit	Timing	Dose	Vaccine [1]	Route [2]	Site	Side
1	Vacc 1 at Day 0	1	FLU Q-QIV or *Fluarix*-VB or *Fluarix*-YB	IM	#Deltoid muscle/anterolateral thigh	#Left (or non-dominant)
2	Vacc 2* at Day 28	2*	FLU Q-QIV or *Fluarix*-VB or *Fluarix*-YB	IM	#Deltoid muscle/anterolateral thigh	#Left (or non-dominant)

1. Vaccine/ Control
2. IM = Intramuscular
Vacc = Vaccination
# deltoid region of the arm for children ≥12 months of age; antero-lateral region of the thigh for infants <12 months of age
*for unprimed children only

The vaccinees were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccine(s).

5.4.3. Treatment allocation and randomization

5.4.3.1. Randomization of supplies

The randomization list was generated at GSK Biologicals, Rixensart, using a standard SAS® (Statistical Analysis System, Cary, NC, USA) program (MATEX) and was used to number the vaccines. A randomization blocking scheme (1:1) was used to ensure that balance between treatments was maintained throughout the study and a treatment number was used to uniquely identify the vaccine dose to be administered to the same subject. The transfer of supplies to the study centers was tracked in the central randomization system.

To allow GSK Biologicals to take advantage of greater rates of recruitment than anticipated at individual centers in this multi-center study, and thus to reduce the overall study recruitment period, an over-randomization of supplies was prepared.

The vaccine doses were to be distributed to each study center while respecting the randomization block size.

5.4.3.2. Randomization of subjects

The treatment allocation at the investigator sites was performed using an internet-based central randomization system (SBIR). The target was to enrol approximately 2700 eligible subjects, 3 to 17 years old, to be randomly assigned to three study groups (FLU Q-QIV, *Fluarix*-VB, and *Fluarix*-YB) in a 1:1:1 ratio, i.e., with approximately 900 subjects in each group. Subjects were stratified by age into two groups (3 to 8 years old, and 9 to 17 years old). The randomization algorithm used a minimization procedure which accounted for prior vaccine priming status, country, and the age sub-segments of 3 to 4 years and 5 to 8 years which were all considered as minimization factors. Minimization factors had equal weight in the minimization algorithm.

An additional 300 eligible subjects, 6 to 35 months old, were enrolled in a separate and independent, open-label, FLU Q-QIV-only arm of the study. There was no age stratification in the 6 to 35 month old age group.

After having checked that a subject was eligible, and after informed consent had been obtained from the parent/LAR, the person in charge of the vaccination accessed the randomization system on the Internet to receive a treatment number. Upon providing the age, the priming status, and the subject identification number, the randomization system used the minimization algorithm to determine the treatment assignment for the subject. The lowest treatment number corresponding to the assigned treatment and available among vaccine doses at the site was then issued to the person in charge of the vaccination.

The actual treatment number used for the subject was to be recorded by the investigator on the eCRF.

5.4.4. Blinding

The comparison of FLU Q-QIV to the *Fluarix* vaccines in 3 to 17 year old subjects was carried out in a double-blinded manner, that is, the subjects (and their parents/LARs), the investigator, and sponsor staff who were involved in the treatment or clinical evaluation of the subjects and review/analysis of study data were all unaware of the treatment assignments.

The serological data, which would lead to the unblinding of the treatment groups, was not available during the course of the study to any investigator or any person involved in the clinical conduct of the study (including data cleaning).

The descriptive evaluation of FLU Q-QIV in 6 to 35 months old subjects was open-label.

Since the separate, open-label, FLU Q-QIV only group was an independent and stand-alone arm with no contribution to the primary study objectives and there were no analytical plans to include data from the open-label arm with the analysis of data from the other three blinded arms, the overall blinding for this study was effectively considered to be double-blind.

The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

5.5. Prior and concomitant medication /vaccinations

- At each study visit, the investigator was to question the subject and/or the subject's parents/LAR about any medication(s) taken and vaccination received by the subject 30 days prior to the first visit/study vaccination, on the day of vaccination and post-vaccination.
- All concomitant medications, with the exception of vitamins and/or dietary supplements, administered at any time during the period starting with administration

of each dose of study vaccine and up to 28 days after each dose of study vaccine were to be recorded in the eCRF with the generic name of the medication (trade names were allowed for combination drugs, i.e. multi-component drugs), medical indication, total daily dose, route of administration, start and end dates of treatment.

- Any treatments and/or medications specifically contraindicated, e.g., any immunoglobulins, other blood products and any immune modifying drugs administered within or 3 months prior to vaccination or at any time during the study period were to be recorded with the generic name of the medication (trade names were allowed for combination drugs only), medical indication, total daily dose, route of administration, start and end dates of treatment.
- Any vaccine not foreseen in the study protocol administered in the period beginning 30 days preceding each dose of study vaccine and up to 27 days after each dose of study vaccine was to be recorded in the eCRF with the trade name, route of administration and date(s) of administration.
- A prophylactic medication was a medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination (e.g., an anti-pyretic is considered to be prophylactic when it is given in the absence of fever and any other symptom, to prevent fever from occurring). Given that an important goal of the study was to assess the tolerability of the study vaccine, the use of prophylactic medications (other than a topical anesthetic at the injection site) to prevent or pre-empt symptoms due to vaccination was discouraged.
- During the period starting with administration of each dose of study vaccine and through the final study contact at Day 180, concomitant medication administered for the treatment of an MAE or pIMD had to be recorded in the eCRF with the generic name of the medication (trade names were allowed for combination drugs only), medical indication (including which MAE or pIMD), total daily dose, route of administration, start and end dates of treatment. Similarly, concomitant medication administered for the treatment of an SAE, at any time during the extended safety follow up period (180 days), had to be recorded on the SAE screens in the eCRF, as applicable.
- During the period starting with administration of each dose of study vaccine and through the final study contact at Day 180, administration of Coumadin derivatives or heparin had to be recorded in the eCRF.
- Any investigational medication or vaccine administered throughout the study (i.e., from Day 0 through the final safety follow-up visit which was approximately 180 days after the first dose) was to be recorded in the eCRF.

5.6. Laboratory assays and time points

All Serological assays for the determination of antibodies against influenza virus components will be performed at GSK Biologicals' laboratory or in a validated laboratory designated by GSK Biologicals using standardized and validated procedures (Table 6).

Table 6 Laboratory assays

System	Component§	Scale	Method	Kit/ Manufacturer	Unit	Cut-off	Laboratory
Serum	**H1N1 strain:** A/California/7/2009 NYMC X-181 (H1N1)-	Quantitative	Hemagglutination-inhibition	In-house assay	1/dilution	10	GSK Biologicals*
Serum	**H1N1 strain:** A/California/7/2009 NYMC X-179A (H1N1)-	Quantitative	Hemagglutination-inhibition	In-house assay	1/dilution	10	GSK Biologicals*
Serum	**H3N2 strain:** A/Victoria/210/2009 (an A/Perth/16/2009 [H3N2]-like virus)	Quantitative	Hemagglutination-inhibition	In-house assay	1/dilution	10	GSK Biologicals*
Serum	**Victoria lineage B strain:** B/Brisbane/60/2008	Quantitative	Hemagglutination-inhibition	In-house assay	1/dilution	10	GSK Biologicals*
Serum	**Yamagata lineage B strain:** B/Brisbane/3/2007	Quantitative	Hemagglutination-inhibition	In-house assay	1/dilution	10	GSK Biologicals*
Serum	**Yamagata lineage B strain:** B/Florida/4/2006	Quantitative	Hemagglutination-inhibition	In-house assay	1/dilution	10	GSK Biologicals*

*GSK Biologicals laboratory or validated laboratory designated by GSK Biologicals; 1/dilution = reciprocal of the dilution

The GSK Biologicals' clinical laboratories have established a Quality System supported by procedures. The activities of GSK Biologicals' clinical laboratories are audited regularly for quality assessment by an internal (sponsor-dependent) but laboratory-independent Quality Department.

5.7. Assessment of immunogenicity variables

Pre- and post-vaccination blood samples were collected for measurement of HI antibody response for all vaccine strains (see Table 7).

Table 7 Summary of blood sampling time points and assays for the assessment of immunology variables

Blood sampling timepoint		Treatment group	No. of subjects	*Component	Components priority rank
Type of contact and timepoint	Sampling timepoint				
Visit 1 (Day 0)	Pre-Vacc	Q-QIV-1 + Q-QIV-2	~1200	A/California/7/2009 NYMC X-179A (H1N1) A/Victoria/210/2009 (an A/Perth/16/2009 [H3N2]-like virus) B/Brisbane/60/2008 B/Florida/4/2006	1
		TIV-VB	~900	A/California/7/2009 NYMC X-181 (H1N1) A/Victoria/210/2009 (an A/Perth/16/2009 [H3N2]-like virus) B/Brisbane/60/2008	1
		TIV-YB	~900	A/California/7/2009 NYMC X-181 (H1N1) A/Victoria/210/2009 (an A/Perth/16/2009 [H3N2]-like virus) B/Brisbane/3/2007	1
Visit 2 and Visit 3 (Day 28 and Day 56)	Post-Vacc 1 and Post-Vacc 2	Q-QIV-1 + Q-QIV-2	~1200	Same as for Q-QIV-1 + Q-QIV-2 groups above	1
		TIV-VB	~900	Same as for TIV-VB group above	1
		TIV-YB	~900	Same as for TIV-YB group above	1

Visit 1 (Day 0), Pre-Vacc: blood sampling at this visit/timepoint will be for all subjects
Visit 2 (Day 28), Post-Vacc 1: blood sampling at these visits/timepoints will be only for primed subjects
Visit 3 (Day 56), Post-Vacc 2: blood sampling at these visits/timepoints will be only for unprimed subjects

5.7.1. Immunological correlates of protection

Although there is no accepted correlate of immunity against influenza with respect to specific levels of HA-specific antibody titer post-vaccination induced with inactivated influenza virus vaccines, the protective role of antibodies against HA and, to a lesser extent, neuraminidase, is well established and has been demonstrated both in experimentally infected animals and humans (Brydak, 2000). For this reason, the induction of antibodies is used as marker of potential vaccine efficacy and the serum HI assay is used to demonstrate this humoral response. HI antibody titers of 1:40 or greater have been associated with protection from influenza illness in at least 50% of adult subjects in some human challenge studies (Hannoun, 2004; Hobson , 1972). While the

1:40 titer is termed "seroprotection" for convenience, it is recognized that no association of this titer with protection has been formally demonstrated in children.

5.8. Assessment of safety variables

The investigator or site staff was/were responsible for the detection and documentation of events meeting the criteria and definition of an adverse event (AE) or serious adverse event (SAE) as provided in the protocol. During the study, in the event of a safety evaluation, the investigator or site staff was/were responsible for detecting AEs and SAEs.

Each subject's parents/LAR was instructed to contact the investigator immediately should the subject have manifested any signs or symptoms they perceived as serious or indicating a substantial change in the subject's health status.

5.8.1. Adverse events

An adverse event (AE) was defined as any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.

Examples of an AE included:

- Significant or unexpected worsening or exacerbation of the condition/indication under study.
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after investigational product administration even though it may have been present prior to the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either investigational product or a concurrent medication (overdose per se should not be reported as an AE/SAE).
- Significant failure of expected pharmacological or biological action.
- Signs and/or symptoms temporally associated with vaccine administration.

Examples of an AE DID NOT include:

- Medical or surgical procedure (e.g., endoscopy, appendectomy); however, the condition that leads to the procedure is considered an AE.

- Situations where an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).

- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that did not worsen.

AEs may have included pre- or post-treatment events that occurred as a result of protocol-mandated procedures (i.e. invasive procedures, modification of a subject's pervious therapeutic regimen).

AEs recorded as endpoints were solicited events. All other AEs were recorded as unsolicited AEs (spontaneous AEs).

Example of events recorded in the medical history section of the CRF/eCRF:

- Pre-existing conditions or signs and/or symptoms present in a subject prior to the start of the study (i.e. prior to the first study vaccination).

All solicited local (injection site) reactions were considered causally related to vaccination.

Solicited adverse events

Solicited symptoms were to be recorded by the parent/LAR of the subject using a diary card. Solicited symptoms (Table 8) occurring during the 7-day follow-up period after vaccination (day of vaccination and 6 subsequent days) was to be recorded in the appropriate section of the eCRF. The investigator was to record, on the eCRF, any analgesics and/or antipyretics taken by the subject to correct the symptoms (local and/or general) during the 7-day follow-up period after vaccination.

The following local (injection-site) and general adverse events were solicited:

Table 8 Solicited local and general AEs

Solicited local (injection site) AEs: In All Subjects	Solicited general AEs	
	In Subjects < 5 years of age	In Subjects ≥ 5 years of age
Pain	Drowsiness	Fatigue/tiredness
Redness	Fever	Fever
Swelling	Irritability/ Fussiness	Headache
	Loss of appetite	Joint pain
		Muscle aches (generalized/widespread)
		Shivering
		Gastrointestinal symptoms †

†Gastrointestinal symptoms include nausea, vomiting, diarrhea and/or abdominal pain.

Temperature was to be recorded in the evening. The parent/LAR should have taken their child's temperature at other times if they believed their child might be feverish (oral temperature equal or over 38°C). Should additional temperature measurements have had to be performed at other times of the day, the highest temperature in each 24-hour period was to be entered into the diary card and eCRF.

Assessment of intensity

Intensity of the following AEs was assessed as described in Table 9.

Table 9 Intensity scales for solicited symptoms in children younger than 5 years of age

Infant/Toddler/Child (< 5 years)		
Adverse Event	**Intensity grade**	**Parameter**
Pain at injection site	0	None
	1	Mild: Minor reaction to touch
	2	Moderate: Cries/protests on touch
	3	Severe: Cries when limb is moved/spontaneously painful
Redness at injection site		Record greatest surface diameter in mm
Swelling at injection site		Record greatest surface diameter in mm
Fever*		Record temperature in °C/°F
Irritability/Fussiness	0	Behavior as usual
	1	Mild: Crying more than usual/no effect on normal activity
	2	Moderate: Crying more than usual/interferes with normal activity
	3	Severe: Crying that cannot be comforted/prevents normal activity
Drowsiness	0	Behavior as usual
	1	Mild: Drowsiness easily tolerated
	2	Moderate: Drowsiness that interferes with normal activity
	3	Severe: Drowsiness that prevents normal activity
Loss of appetite	0	Appetite as usual
	1	Mild: Eating less than usual/no effect on normal activity
	2	Moderate: Eating less than usual/interferes with normal activity
	3	Severe: Not eating at all

*Fever was defined as temperature ≥ 38.0°C or 100.4°F measured by any method

Table 10 Intensity scales for solicited symptoms in children 5 years of age or older

Adolescents/Child (≥ 5 years)		
Adverse Event	**Intensity grade**	**Parameter**
Pain at injection site	0	None
	1	Mild: Any pain neither interfering with nor preventing normal every day activities.
	2	Moderate: Painful when limb is moved and interferes with every day activities.
	3	Severe: Significant pain at rest. Prevents normal every day activities.
Redness at injection site		Record greatest surface diameter in mm
Swelling at injection site		Record greatest surface diameter in mm
Fever*		Record temperature in °C/°F
Headache	0	Normal
	1	Mild: Headache that is easily tolerated
	2	Moderate: Headache that interferes with normal activity
	3	Severe: Headache that prevents normal activity
Fatigue	0	Normal
	1	Mild: Fatigue that is easily tolerated
	2	Moderate: Fatigue that interferes with normal activity
	3	Severe: Fatigue that prevents normal activity
Gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain)	0	Gastrointestinal symptoms normal
	1	Mild: Gastrointestinal symptoms that are easily tolerated
	2	Moderate: Gastrointestinal symptoms that interfere with normal activity
	3	Severe: Gastrointestinal symptoms that prevent normal activity
Joint pain, muscle aches, shivering	0	Normal
	1	Mild: that is easily tolerate
	2	Moderate: that interferes with normal activity
	3	Severe: that prevents normal activity

*Fever was defined as temperature ≥ 38.0°C or 100.4°F measured by any method

The maximum intensity of local injection site redness/swelling/induration was scored as follows:

0 : ≤ 20 mm
1 : > 20 - ≤ 50 mm
2 : > 50 - ≤ 100 mm
3 : > 100 mm

The maximum intensity of temperature was scored as follows:

0 < 38.0°C (100.4°F)
1 : ≥ 38.0 (100.4°F)- < 38.5°C (101.3°F)
2 : ≥ 38.5 (101.3°F)- < 39.0°C (102.2°F)
3 : ≥ 39.0 (102.2°F)- ≤ 40°C (104°F)
4 > 40°C (104°F) (also reported as an SAE)

The investigator was to make an assessment of the maximum intensity that occurred over the duration of the event for all other AEs, i.e. unsolicited symptoms, including SAEs reported during the study. The assessment was to be based on the investigator's clinical judgment. The intensity of each AE and SAE recorded in the eCRF or SAE Report screens, as applicable, was to be assigned to one of the following categories:

1 (mild)	=	An AE easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE preventing normal, everyday activities. (In a young child, such an AE would, for example, prevent attendance at school/ kindergarten/ a day-care center and would cause the parent(s)/LAR(s) to seek medical advice. In an adolescent, such an AE would, for example, prevent attendance at work/school and would necessitate the administration of corrective therapy)

An AE assessed as Grade 3 (severe) should not be confused with an SAE. Grade 3 is a category utilized for rating the intensity of an event; both AEs and SAEs could be assessed as Grade 3. An event was defined as 'serious' when it met one of the pre-defined outcomes described in Section 5.8.3.

Assessment of causality:

The investigator was obligated to assess the relationship between investigational product and the occurrence of each AE/SAE. The investigator was to use clinical judgment to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational product were to be considered and investigated. The investigator was also to consult the Investigator Brochure and/or Product Information, for marketed products, in the determination of his/her assessment.

There may have been situations in which an SAE occurred and the investigator had minimal information to include in the initial report to GSK Biologicals. However, it was very important that the investigator always made an assessment of causality for every event prior to transmission of the SAE Report Form to GSK Biologicals. The investigator may subsequently have changed his/her opinion of causality in light of follow-up information, amending the SAE Report Form accordingly. The causality assessment was one of the criteria used when determining regulatory reporting requirements.

All solicited local (injection site) reactions were to be considered causally related to vaccination. Causality of all other AEs was to be assessed by the investigator using the following question:

"Is there a reasonable possibility that the AE may have been caused by the investigational product?"

NO The AE is not causally related to administration of the study vaccine. There are other, more likely causes and administration of the study vaccine is not suspected to have contributed to the AE.

YES There is a reasonable possibility that the vaccine contributed to the AE.

Non-serious and serious AEs were to be evaluated as two distinct events. If an event met the criteria to be determined "serious," it was examined by the investigator so that ALL contributing factors applicable to each SAE could be determined.

- Other possible contributors included:
- Medical history,
- Other medication,
- Protocol required procedure,
- Other procedure not required by the protocol,
- Lack of efficacy of the vaccine*, if applicable,
- Erroneous administration,
- Other cause (investigator specified).

(*"Lack of efficacy" was not reported as an AE. "Efficacy" in this trial was measured as an immune response to the virus vaccine strains. Lack of such efficacy was without signs, symptoms, or sequelae in the absence of virus circulation at the time the study was done and therefore not consistent with an AE).

5.8.2. Medically attended visits

For each solicited and unsolicited symptom the subject experienced, the subject/subject's parent(s)/LAR(s) was to be asked if they received medical attention defined as hospitalization, an emergency room visit or a visit to or from medical personnel (medical doctor) for any reason and this information was to be recorded in the eCRF. In some countries, nurse practitioners or healthcare workers, not doctors, may have been the first point of contact. However, this was not to be applicable to solicited symptom(s) which require contact with the investigator/study personnel.

Medical visits attended for routine check-ups were not to be recorded in the eCRF.

5.8.3. Serious adverse events

A serious adverse event (SAE) was any untoward medical occurrence that:

a. resulted in death,

b. was life-threatening,

NOTE: The term 'life-threatening' in the definition of 'serious' refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.

c. required hospitalization or prolongation of existing hospitalization,

NOTE: In general, hospitalization signifies that the subject was detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or out-patient setting. Complications that occurred during hospitalization were AEs. If a complication prolonged hospitalization or fulfilled any other serious criteria, the event was serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE was to be considered serious.

Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline was not considered an AE.

d. resulted in disability/incapacity, or

NOTE: The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition was not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g. sprained ankle) which may have interfered or prevented everyday life functions but did not constitute a substantial disruption.

e. was a congenital anomaly/birth defect in the offspring of a study subject.

Medical or scientific judgment was to be exercised in deciding whether reporting was appropriate in other situations, such as important medical events that may not have been immediately life-threatening or resulted in death or hospitalization but may have jeopardized the subject or may have required medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These were also to be considered serious. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalization.

Clinical laboratory parameters and other abnormal assessments qualifying as adverse events and serious adverse events

Abnormal laboratory findings (e.g. clinical chemistry, hematology, urinalysis) or other abnormal assessments that were judged by the investigator to be clinically significant were to be recorded as AEs or SAEs if they met the definition of an AE or SAE. Clinically significant abnormal laboratory findings or other abnormal assessments that were detected during the study or were present at baseline and significantly worsened following the start of the study were to be reported as AEs or SAEs. However, clinically significant abnormal laboratory findings or other abnormal assessments that are associated with the disease being studied, unless judged by the investigator as more severe than expected for the subject's condition, or that are present or detected at the start of the study and did not worsen, were not to be reported as AEs or SAEs.

The investigator was to exercise his or her medical and scientific judgment in deciding whether an abnormal laboratory finding or other abnormal assessment was clinically significant.

Time period, frequency, and method of detecting adverse events and serious adverse events

All AEs occurring within 28 days following administration of each dose of vaccine/ comparator were to be recorded on the Adverse Event form in the subject's eCRF, irrespective of intensity or whether or not they were considered vaccination-related.

All reports of convulsion (seizure) or fever ≥39˚C (102.2˚F) occurring in any subject <5 years of age within 2 days of vaccination (i.e. day of vaccination and following day) were to be reported in the e-CRF within 24 hours.

The standard time period for collecting and recording SAEs was to begin at the first receipt of study vaccine/comparator and end 180 days following administration of the last dose of study vaccine/comparator for each subject.

Additionally, all medically attended AEs and SAEs occurring during the period starting from the day of vaccination and ending at six months (minimum 180 days) had to be recorded.

In addition to the above-mentioned reporting requirements and, in order to fulfill international reporting obligations, SAEs that were related to study participation (e.g. protocol-mandated procedures, invasive tests, a change from existing therapy) or were related to a concurrent GSK medication were to be collected and recorded from the time the subject’s parents/LAR consented to participate in the study to the time the subject was discharged.

All cases of pregnancy during the entire study period (Day 0 to Day 180) had to be reported using the pregnancy report form.

The investigator was to inquire about the occurrence of AEs/SAEs at every visit during the study.

All AEs either observed by the investigator or one of his clinical collaborators or reported by the subject’s parents/LAR spontaneously or in response to a direct question were to be evaluated by the investigator. AEs not previously documented in the study were to be recorded in the Adverse Event form within the subject's eCRF. The nature of each event, date and time (where appropriate) of onset, outcome, intensity and investigator’s assessment of relationship to vaccine was to be established. Details of any corrective treatment were to be recorded on the appropriate page of the eCRF.

As a consistent method of soliciting AEs, the subject’s parents/LAR was to be asked a non-leading question such as:

"*Has your child acted differently or felt different in any way since receiving the vaccine or since the last visit*?"

N.B. The investigator was to record only those AEs having occurred within the time frame defined in the protocol.

AEs already documented in the eCRF, i.e. at a previous assessment, and designated as "not recovered/not resolved" or "recovering/resolving" were to be reviewed at subsequent visits, as necessary. If these had resolved, the documentation in the eCRF was to be completed.

When an AE/SAE occurred, it was the responsibility of the investigator to review all documentation (e.g. hospital progress notes, laboratory, and diagnostics reports) relative to the event. The investigator was then to record all relevant information regarding an AE/SAE on the eCRF. It was not acceptable for the investigator to send photocopies of the subject's medical records to GSK Biologicals in lieu of the appropriate completed AE/SAE pages/SAE screens in the eCRF. However, there may have been instances when copies of medical records for certain cases were requested by GSK Biologicals. In this instance, all subject identifiers were to be blinded on the copies of the medical records prior to submission to GSK Biologicals.

The investigator was to attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis and not the individual signs/symptoms was to be documented as the AE/SAE.

The electronic system using SAE screens in the eCRF was to be the primary mode for reporting SAEs to GSK Biologicals during the study period. In case the electronic system for reporting SAEs did not work or after freezing of the subject's eCRF, paper SAE Report Forms and the facsimile (Fax) system were to be used to report SAEs.

Follow-up of adverse events and serious adverse events and assessment of outcome

After the initial AE/SAE report, the investigator was required to proactively follow each subject and provide further information to GSK Biologicals on the subject's condition.

All AEs and SAEs documented at a previous visit and designated as not recovered/not resolved or recovering/resolving were to be reviewed at subsequent visits. All SAEs were to be followed up until the end of the study and all AEs were to be followed up until 30 days after the last vaccination.

Investigators were to follow-up subjects:

- with SAEs or subjects withdrawn from the study as a result of an AE, until the event had resolved, subsided, stabilized, disappeared, the event was otherwise explained, or the subject was lost to follow-up;
- or, in the case of non-serious medically attended AEs, until the subjects had completed the study or they were lost to follow-up;
- or, in the case of other non-serious AEs, until completion of the Day 28 visit (primed subjects) or of the Day 56 visit (unprimed subjects).

Clinically significant laboratory abnormalities were to be followed up until they had returned to normal, or a satisfactory explanation had been provided. Additional information (including but not limited to laboratory results) relative to the subsequent course of such abnormalities noted for any subject was to be made available to the Site Monitor.

GSK Biologicals may have requested that the investigator perform or arrange for the conduct of supplemental measurements and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE or SAE. The investigator would then have been obliged to assist. If a subject died during participation in the study or during a recognized follow-up period, GSK Biologicals was to be provided with a copy of any available post-mortem findings, including histopathology.

New or updated information was to be recorded on the originally completed SAE Report Form, with all changes signed and dated by the investigator. The updated SAE report form was to be resent to GSK Biologicals within 24 hours of receipt of the follow-up information.

In case the electronic SAE reporting system did not work or after freezing of the subject's eCRF, paper SAE Report Forms and the facsimile (Fax) system were to be used to report SAEs.

The outcome of any non-serious AE occurring within 28 days post-vaccination (i.e. unsolicited AE) or any SAE reported during the entire study was to be assessed as:

- Recovered/resolved,
- Not recovered/not resolved,
- Recovering/resolving,
- Recovered with sequelae/resolved with sequelae,
- Fatal (SAEs only).

Time frames for submitting serious adverse event reports to GSK Biologicals

SAEs were to be reported promptly to GSK Biologicals once the investigator determined that the event met the protocol definition of an SAE. The investigator was to complete and submit relevant information on the SAEs in the SAE screens in eCRF within 24 hours of his/her becoming aware of these events. Additional or follow-up information relating to the initial SAE report was also to be completed and submitted in the SAE screens in eCRF within 24 hours of receipt of such information.

When paper SAE Report Form was used as back-up system (if the electronic SAE reporting system did not work or after freezing of the subject's eCRF), the investigator was to fax the SAE reports directly to the GSK Central Safety department within 24 hours. During the study, the investigator was to update the SAE screens in eCRF once the electronic system was working again (and not later than 24 hours) and before using it to report additional information.

The investigator was always required to provide an assessment of causality at the time of the initial report.

The SAE Report Form was always to be completed as thoroughly as possible with all available details of the event, signed by the investigator (or designee), and forwarded to GSK Biologicals within the designated time frames. If the investigator did not have all information regarding an SAE, he/she was not to wait to receive additional information before notifying GSK Biologicals of the event and completing the form. When additional information was received on a SAE reported to GSK Biologicals using the back-up paper SAE Report Form during the study period, the electronic system was to be used to report the additional information within 24 hours if the electronic system was working again and only after updating the SAE screens in eCRF once the electronic system was working again.

When additional information was received on a SAE after freezing of the subject's eCRF, new or updated information was to be recorded on the paper SAE Report Form, with all changes signed and dated by the investigator. The updated SAE Report Form was to be resent to GSK Biologicals within 24 hours of receipt of the follow-up information.

In rare circumstances, if the electronic system for reporting SAEs did not work and in the absence of facsimile equipment, notification by telephone was acceptable, with a copy of the SAE Report Form sent by email or by mail. Initial notification via telephone did not replace the need for the investigator to complete and submit SAE screens in the eCRF (or complete and sign the SAE Report Form if the back-up system needed to be used).

In the event of a death determined by the investigator to be related to vaccination, completion of SAE screens in the eCRF/sending of the fax (if the electronic SAE reporting system did not work or after freezing of the subject's eCRF) was to be accompanied by a telephone call to the Study Contact for Faxing/Reporting SAEs.

Regulatory reporting requirements for serious adverse events

The investigator was to promptly report all SAEs to GSK Biologicals in accordance with the procedures detailed in the protocol. GSK Biologicals has a legal responsibility to promptly notify, as appropriate, both the local regulatory authority and other regulatory agencies about the safety of a product under clinical investigation. Prompt notification of SAEs by the investigator to the Study Contact for Reporting SAEs was essential so that legal obligations and ethical responsibilities towards the safety of other subjects could be met.

The investigator, or responsible person according to local requirements, was to comply with the applicable local regulatory requirements related to the reporting of SAEs to the IRB/IEC and, if required, to the applicable government authority.

Investigator safety reports were prepared according to the current GSK Biologicals policy and were forwarded to investigators as necessary. An investigator safety report was prepared for an SAE(s) that is both attributable to investigational product and unexpected. The purpose of the report was to fulfil specific regulatory and Good Clinical Practice (GCP) requirements, regarding the product under investigation.

An investigator who received an investigator safety report describing a SAE(s) or other specific safety information (e.g. summary or listing of SAEs) from GSK Biologicals was to file it with the Investigator Brochure or other appropriate study documentation and was to notify the IRB or IEC, if appropriate according to local requirements.

Post-study adverse events and serious adverse events:

A post-study AE/SAE is defined as any event that occurred outside of the AE/SAE detection period defined in the protocol. Investigators were not obligated to actively seek AEs or SAEs in former study participants.

However, if the investigator learned of any SAE, including a death, at any time after a subject had been discharged from the study, and he/she considered the event reasonably related to the investigational product, the investigator was to promptly notify the Study Contact for Reporting SAEs.

After freezing of the subject's eCRF, if SAE follow-ups or new SAEs had to be reported, the investigators or designate were to use paper SAE Report Forms and the facsimile (Fax) system.

Treatment of adverse events:

Treatment of any adverse event was at the sole discretion of the investigator and according to current good medical practice. Any medication administered for the treatment of an AE was to be recorded in the subject's eCRF.

5.8.4. Potential immune-mediated diseases

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology - both of which are listed below. GSK required Investigators to report such adverse events within the same time limits (following confirmation of an AE as a pIMD; see last paragraph of this section below), and using the same eCRF pages, as utilized for SAEs. A field was available with the SAE eCRF pages which allowed the investigator to specify that the event was a pIMD, but did not otherwise fulfill the criteria which characterize an SAE. The investigator was to evaluate the occurrence of pIMDs at every visit/contact during the study. GSK also expected investigators to provide additional information about pIMD events. AEs to be reported and documented as pIMDs included:

- **Neuroinflammatory disorders:** optic neuritis, cranial nerve disorders (including Bell's palsy), multiple sclerosis, demyelinating disease, transverse myelitis, Guillain-Barré syndrome, myasthenia gravis, encephalitis, neuritis.
- **Musculoskeletal disorders:** systemic lupus erythematosus, cutaneous lupus, Sjögren's syndrome, scleroderma, dermatomyositis, polymyositis, rheumatoid arthritis and juvenile rheumatoid arthritis, polymyalgia rheumatica or temporal arteritis, reactive arthritis, psoriatic arthropathy, ankylosing spondylitis, undifferentiated spondyloarthropathy.

- **Gastrointestinal disorders:** Crohn's disease, ulcerative colitis or proctitis, celiac disease.
- **Metabolic diseases:** autoimmune thyroiditis, Grave's or Basedow's disease, Hashimoto thyroiditis, insulin-dependent diabetes mellitus (IDDM), Addison's disease.
- **Skin disorders:** psoriasis, vitiligo, Raynaud's phenomenon, erythema nodosum, autoimmune bullous skin diseases.
- **Others:** autoimmune hemolytic anemia, thrombocytopenia, antiphospholipid syndrome, *vasculitis, pernicious anemia, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, autoimmune glomerulonephritis, autoimmune uveitis, autoimmune myocarditis/cardiomyopathy, sarcoidosis, Stevens-Johnson syndrome, Behçet's syndrome.

*Vasculitis: Vasculitis, Diffuse vasculitis, Leucocytoclastic vasculitis, Polyarteritis nodosa, Microscopic polyangiitis, Wegener's granulomatosis, Anti-neutrophil cytoplasmic antibody positive vasculitis, Henoch-schönlein purpura, Allergic granulomatous angiitis (Churg-Strauss disease), Kawasaki disease, Takayasu's arteritis, Temporal arteritis(Giant cell arteritis), Renal vasculitis.

Medical judgment was to be exercised in deciding whether other disorders/diseases may have had an autoimmune origin and they were to have been reported as described above, and this was the investigator's prerogative. Whenever sufficient data existed to substantiate any of the diagnoses in the above list, it had to be reported as a pIMD. While the intent of pIMD reporting is to be inclusive, isolated nonspecific symptoms, which might (or might not) have represented the above diagnoses, were to be captured as AEs but not reported as pIMDs until the diagnosis could be defended.

5.8.5. Pregnancy

The investigator, or his/her designee, was to collect pregnancy information on any subject who became pregnant while participating in this study. The investigator, or his/her designee, was to record pregnancy information on the Pregnancy Report Form and submit it to GSK Biologicals within 24 hours of learning of a subject's pregnancy. The subject was to be followed to determine the outcome of the pregnancy. At the end of the pregnancy, whether full-term or premature, information on the status of the mother and child was to be forwarded to GSK Biologicals. Generally, follow-up was to be no longer than six to eight weeks following the estimated delivery date.

While pregnancy itself was not considered an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons was to be recorded as an AE or a SAE, and was to be followed. A spontaneous abortion was always considered to be an SAE and was to be reported. Furthermore, any SAE occurring as a result of a post-study pregnancy and considered reasonably related in time to receipt of the investigational product by the investigator, was to be reported to GSK Biologicals. While the investigator was not obligated to actively seek this information from former study participants, he/she may have learned of a pregnancy through spontaneous reporting.

Information on pregnancies identified during the screening phase/prior to vaccine administration did not need to be collected and communicated to safety.

5.9. Data quality assurance

To ensure that the study procedures conformed across all investigator sites, the protocol, case report form, and safety reporting were reviewed with the investigator(s) and his/her/their personnel responsible for the conduct of the study by the Company representative(s) prior to study start.

Adherence to the protocol requirements and verification of data generation accuracy were achieved through monitoring visits to each investigator site. Computer checks and blinded review of subject tabulations were performed to ensure consistency of CRF/eCRF completion. All procedures were performed according to methodologies detailed in GlaxoSmithKline Biologicals Standard Operating Procedures (SOPs).

Independent Audit statement:

This study was subject to audit by GlaxoSmithKline's department of Worldwide Regulatory Compliance-GCP (WRC-GCP).

5.10. Statistical methods

The statistical analyses were performed as specified in the protocol except for the changes from protocol described in Section 5.11.

The following group names will be used for the statistical analyses:

Group order in tables	Group label in tables	Group definition for footnote
1	QIV1	FLU Q-QIV (3 - 17 year old subjects)
2	TIV-VB	*Fluarix* TIV Victoria B strain (3 - 17 year old subjects)
3	TIV-YB	*Fluarix* TIV Yamagata B strain (3 - 17 year old subjects)
4	QIV2	FLU Q-QIV (6 - 35 months old subjects)

5.10.1. Primary endpoint

Humoral immune response to each of the influenza vaccine. Serum hemagglutination inhibiting (HI) antibodies 28 days after the last vaccine dose will be used to calculate:

- *GMTs of HI antibody titers
- *SCR

*See glossary for definitions of GMT and SCR.

5.10.2. Secondary endpoints

Humoral immune response in each vaccine group overall and by age (6 to 35 months old, 3 to 8 years old, and 9 to 17 years of age). Serum anti-HA antibody titers against the 4 vaccine strains at Day 0 and 28 days after last vaccine dose will be used to calculate:

- *GMTs
- *SCRs
- *SPRs
- *SCFs

*See glossary for definitions of GMT, SCR, SPR, and SCF.

Solicited local adverse events:

- Incidence rate, duration, and intensity during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after each vaccination in each group.

Solicited general adverse events:

- Incidence rate, duration, intensity, and relationship to vaccination during a 7-day follow-up period (i.e. day of vaccination and 6-subsequent days) after each vaccination in each group.

Unsolicited adverse events:

- Incidence rate, intensity, and relationship to vaccination of unsolicited adverse events during a 28-day follow-up period (i.e. day of vaccination and 27 subsequent days) after each vaccination, in each group.

Medically-attended adverse events (MAEs), serious adverse events (SAEs), and potential immune-mediated diseases (pIMDs):

- Incidence rate and relationship to vaccination during a 181 day follow-up period (i.e. day of vaccination and 180 subsequent days) after vaccination in each group.

5.10.3. Determination of sample size

5.10.3.1. Primary objective

- To assess the immunological non-inferiority (in terms of HI antibody GMTs and SCRs) of FLU Q-QIV compared to *Fluarix*-YB (TIV-YB) and *Fluarix*-VB (TIV-VB).

Table 11 shows the power to detect non-inferiority in HI antibody GMTs and Table 12 shows the power to detect non-inferiority in HI antibody SCRs of

- QIV (with 725 subjects) compared to Fluarix-YB + Fluarix-VB (with 1450 subjects) for the two A strains
- QIV (with 725 subjects) compared to Fluarix-VB (with 725 subjects) for the Victoria B strain
- QIV (with 725 subjects) compared to Fluarix-YB (with 725 subjects) for the Yamagata B strain

The sample size of GMT ratio is computed assuming that the upper limit of two-sided 95% confidence interval on the ratio of the GMTs (GMT-FLU TIV/GMT-FLU QIV) at post-vaccination time-point should not exceed 1.5.

The sample size of difference in SCR is computed assuming that the upper limit of the two-sided 95% confidence interval on the difference between the seroconversion rates (SCRTIV – SCRQIV) will not exceed 10%.

Table 11 Statistical power needed to detect immunogenic non-inferiority as assessed by HI antibody GMTs of FLU Q-QIV and *Fluarix*-YB/*Fluarix*-VB using a one-sided, two-sample t-test in subjects aged 3 to 17 years old

Strains	Number of evaluable subjects in FLU QIV group	Number of evaluable subjects in Fluarix-YB/ Fluarix-VB group	Assumed UL of 95% CI on the GMT ratio	StdDev of log (titers)[1]	Power to success (1 test)[2]	Power to success (2 tests)[3]
A strains	725	1450	1.5 fold	0.8	99.80%	99.60%
B strains	725	725	1.5 fold	0.8	98.71%	97.42%

[1] Standard deviation of log (titers) observed in the Fluarix-062 study is 0.66-0.81 (for children aged 6-13 years) and 0.6-0.85 in the Fluarix US-005 study (for children aged 3-5 years)
[2] Power estimated using PASS, One-Sided two-sample t-test for a difference of means, alpha = 2.5%.
[3] Using Bonferroni adjustment on type 2 error (beta)

Table 12 Statistical power needed to detect immunogenic non-inferiority as assessed by seroconversion rates difference between FLU TIV (Fluarix-YB or Fluarix-VB) and FLU QIV using a one-sided-test in subjects aged 3 to 17 years old, and taking 10% as the maximal upper limit of the 95% confidence interval for the difference in seroconversion rates

Strains	Number of evaluable subjects in FLU QIV group	Number of evaluable subjects in FLU TIV group	Proportion in the FLU TIV group[1]	Proportion in the FLU QIV group[2]	Assumed difference in SC rates	Power to success (1 test)[3]	Power to success (2 tests)[4]
A strains	725	1450	0.6	0.6	10%	99.40%	98.80%
B strains	725	725	0.6	0.6	10%	97.35%	94.70%

[1] Seroconversion rate observed in the Fluarix 062 is 0.5-0.85 for children (6-13 years old) and 0.6-0.9 in the Fluarix US-005 in children (3-5 years old)
[2] Estimated seroconversion rate with the FLU-D-QIV vaccine in children 3 to 18 years
[3] Power estimated using PASS, One-Sided t-test on the Difference of proportions, alpha = 2.5%.
[4] Using Bonferroni adjustment on type 2 error (beta)

Therefore, 725 evaluable subjects in each group were needed to obtain an overall power of 90% to achieve the primary objective of non-inferiority. Accounting for an attrition rate of ~20%, a total of 2700 subjects (900 subjects in each group) were required for the primary immunogenicity analysis.

In addition, 300 subjects (aged 6 to 35 months old) were enrolled in the FLU Q-QIV only arm. Accounting for an attrition rate of ~15%, 260 evaluable subjects were expected to be available for the primary immunogenicity analysis.

5.10.3.2. Secondary Objectives

Superiority of the B strain:

Table 13 presents the power analysis to show superiority of the B strain GMT of FLU Q-QIV to Fluarix-YB and Fluarix-VB with 725 evaluable children aged 3 to 17 years in each group for the immunogenicity analysis, using a one-sided two sample t- test and assuming that the lower limit of two-sided 95% confidence interval on the ratio of the GMTs (GMT-FLU-Q-QIV/ GMT Fluarix) at post-vaccination time-point will be at least 1.5.

Table 13 Statistical power needed to detect a difference of 1.5 in the alternate B strain GMT between FLU Q-QIV and FLU-TIV (*Fluarix*-YB or *Fluarix*-VB) using a one-sided two-sample t-test in subjects aged 3 to 17 years old (N = 725 in each group)

Number of evaluable subjects in FLU QIV group	Number of evaluable subjects in FLU TIV group	Assumed difference between GMTs	Standard deviation of log (titers)[1]	Power to success (1 test)[2]	Power to success (2 tests)[3]
725	725	1.6 fold	0.8	99.81%	99.62%

[1]Standard deviation of log (titers) observed in the Fluarix-062 study is 0.66-0.81 (for children aged 6-13 years) and 0.6-0.85 in the Fluarix US-005 study (for children aged 3-5 years)
[2] Power estimated using PASS, One-Sided two-sample t-test for a difference of means, alpha = 2.5%.
[3] Using Bonferroni adjustment on type 2 error (beta)

Table 14 presents the power analysis to show superiority in the B strain seroconversion rates (using a one-sided t-test) between FLU Q-QIV and Fluarix-YB/ Fluarix-VB at Day 28, with 725 evaluable children aged 3 to 17 years in each group for the immunogenicity analysis, assuming the lower limit of the two-sided 95% confidence interval on the difference between the seroconversion rates (SCR-FLU-Q-QIV - SCR-Fluarix) will be at least 10%.

Table 14 Statistical power needed to detect a difference of 10% in the seroconversion rates of the B strains between FLU Q-QIV and FLU-TIV (*Fluarix-YB* or *Fluarix*-VB) using a one-sided t- test (N = 725 in each group) in children aged 3 up to 17 years old, and taking 10% as the minimal lower limit of the 95% confidence interval for the difference in seroconversion rates

Number of evaluable subjects in FLU TIV group	Number of evaluable subjects in FLU QIV group	Proportion in the FLU TIV group[1]	Proportion in the FLU QIV group[2]	Assumed difference in SC rates	Power to success (1 strain)[3]	Power to success (2 tests)[4]
725	725	0.6	0.7	10%	97.95%	95.9%

[1] Seroconversion rate observed in the Fluarix 062 is 0.5-0.85 for children (6-13 years old) and 0.6-0.9 in the Fluarix US-005 in children (3-5 years old)
[2] Estimated seroconversion rate with the FLU-D-QIV vaccine in children 3 to 18 years
[3] Power estimated using PASS, One-Sided t-test on the Difference of proportions, alpha = 2.5%.
[4] Using Bonferroni adjustment on type 2 error (beta)

FDA/CBER criteria:

Table 15 shows the power to meet the secondary objective of achieving the CBER criteria for the alternate, Yamagata B, strain in subjects who receive the FLU Q-QIV vaccine in the 3 to 17 years age group.

Table 15 Statistical power needed to achieve the CBER criteria for HI SCR and SPR for the alternate, Yamagata B, present in FLU Q-QIV in the 3 to 17 years age group with 800 evaluable subjects

Number of evaluable subjects in the FLU Q-QIV group	Criteria	CBER criteria limit	Reference	Power[2] (Beta)
725	SCR	LL ≥ 40%	50%[1]	99.97%
725	SPR	LL≥ 70%	80%[1]	>99.99%

[1]FluLaval 005 study
[2]Power estimated using PASS, One-Sided Exact-test on test for One proportion, alpha=2.5%

5.10.4. Study cohorts /data sets analyzed

Three cohorts were to be evaluated, as described below:

5.10.4.1. Total Vaccinated Cohort (TVC)

The Total Vaccinated cohort (TVC) included all vaccinated subjects for whom data were available. Thus, the TVC for analysis of safety included all subjects with at least one vaccine administration documented and the TVC for analysis of immunogenicity included vaccinated subjects for whom data concerning immunogenicity endpoint measures were available. The TVC analysis was performed per treatment actually administered. This was the primary cohort for analysis of safety.

5.10.4.2. According-To-Protocol (ATP) cohort for analysis of safety (ATP-S)

The ATP cohort for analysis of safety (ATP-S) included all subjects:

- who had received at least one vaccine dose according to their random assignment
- with sufficient data to perform an analysis of safety (at least one vaccine dose according to their random assignment with safety follow-up)
- for whom administration site of study vaccine/comparator was known
- who had not received a vaccine which was not specified or forbidden by the protocol
- for whom the randomization code had not been broken.

5.10.4.3. According-To-Protocol (ATP) cohort for analysis of Immunogenicity (ATP-I)

The ATP cohort for analysis of immunogenicity, in terms of antibody response measured by the HI assay, included all evaluable subjects (i.e., those who met all eligibility criteria, complied with the procedures and intervals defined in the protocol, and did not meet any elimination criteria during the study) for whom data concerning immunogenicity endpoint measures were available. Therefore, this included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination and

- who were within the maximum intervals allowed as defined in the protocol.
- who did not meet any of the criteria for elimination from an ATP analysis during the study
- who did not receive a product leading to exclusion from an ATP analysis
- who did not present with a medical condition leading to exclusion from an ATP analysis
- and for whom the intervals between visits/contacts were strictly followed. These intervals determined each subject's evaluability in the according to protocol analyses.

5.10.5. Derived and transformed data

The cut-off value for antibody titer was defined by the laboratory before the analysis; for this study, the cut-off value was equal to 1:10. A seronegative subject was defined as a subject whose antibody titer was below the cut-off value, and conversely, a seropositive subject was one whose antibody titer was greater than or equal to the cut-off value.

Geometric Mean Titer (GMT) calculations were performed by taking the anti-log of the mean of the log (base 10) transformed inverse titers (the number X would denote the inverse of a titer expressed as "1:X"). Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off value for the purpose of GMT calculation.

Seroprotection Rate (SPR) was defined as the percentage of subjects who had a serum anti-HI antibody titer ≥1:40.

Seroconversion Rate (SCR) was defined as the percentage of vaccinees who had either a pre-vaccination (Day 0) titer <1:10 and post-vaccination reciprocal titer ≥ 1: 40 or a pre-vaccination reciprocal titer ≥1:10 and had at least a 4-fold increase in the post vaccination reciprocal titer.

Seroconversion factor (SCF) was defined as the geometric mean of the within subjects ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer. SCFs were calculated at Day 28 following the complete vaccination regimen.

Incidence rates of AEs were calculated as the number of subjects who reported the event, divided by the number of subjects in the safety analysis cohort (the TVC or ATP for safety analysis cohort).

Handling of missing immunogenicity data: For a given subject and a given immunogenicity measurement, missing or non-evaluable measurements were not to be replaced. Therefore, analyses excluded subjects with missing or non-evaluable measurements.

Handling of missing safety data: For a given subject and the analysis of solicited symptoms within 7 days post-vaccination (Days 0 through 6), missing or non-evaluable measurements were not to be replaced. Therefore the analysis of the solicited symptoms based on the TVC included only vaccinated subjects and doses with documented safety data (i.e., symptom screen/sheet completed). Details of calculation of percentages of subjects with solicited or unsolicited symptoms, as a percentage of doses or per subject, were included in the study Reporting and Analysis Plan.

For the analysis of unsolicited adverse events/medically-attended adverse events/serious adverse events/concomitant medication, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.

For summaries reporting both solicited and unsolicited AEs, all vaccinated subjects were considered. Subjects who did not report the event were considered as subjects without the event.

5.10.6. Analysis of demographics

Demographic characteristics (age, gender, and ethnicity/geographic ancestry) of each study vaccine group and each age group were tabulated. No formal statistical evaluation of treatment group differences with respect to demographic characteristics, were performed.

Summary statistics for subject age classified by gender of the vaccinated subjects, as a whole, and per treatment group, were calculated.

The distribution of subjects enrolled among the study sites were tabulated as a whole and per group, and subjects were classified into disposition categories, including subjects who entered, completed, or withdrew from the study. In addition, the number of subjects in each analysis population, were presented and the number of subjects who received

vaccine were tabulated. Subjects, who were screened but ineligible, as well as those who were excluded from the various analysis sets, were listed in the 'by subject' data listings.

The proportion of subjects with prior immunologic experience with influenza vaccine(s) in the previous 3 influenza seasons were tabulated for each treatment group and categorized by priming status.

5.10.7. Analysis of immunogenicity

The primary analysis was based on the ATP-I cohort. If the percent of vaccinated subjects excluded from this ATP cohort was more than 5%, a second analysis based on the TVC was to be performed to complement the ATP-I analysis.

5.10.7.1. Within groups analysis

For the humoral response in terms of HI antibodies for all vaccine strains, the following parameters were calculated by group for all subjects, each age stratum, and by priming status:

- GMTs of HI at Day 0 and at 28 days following last vaccination with 95% confidence interval (CI)
- SCR at Day 28 following last vaccination with exact 95% CI
- SPR at Day 0 and 28 days following last vaccination with exact 95% CI
- SCF at Day 28 following last vaccination with 95% CI
- CBER criteria were also evaluated

The SCR and SPR immunogenicity endpoints were compared to the following FDA/CBER criteria for vaccine immunogenicity for adults <65 years of age and for the pediatric population) [FDA, 2007]:

Parameter	FDA acceptance criteria**
% Seroconversion rate* or significant increase in titer*	LL of 95% CI ≥40%
% Seroprotection (titer ≥ 40)	LL of 95% CI ≥70%

* Seroconversion defined as: For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer post-vaccination ≥ 4 fold of the pre-vaccination antibody titer
** United States Federal Drug Administration (FDA) criteria for adults < 65 years of age and pediatric population

5.10.7.2. Between groups analysis (Inferential analysis)

Ratio of GMTs:

For each strain, an Analysis of Covariance (ANCOVA) model including vaccine group (Q-QIV, TIV-VB and TIV-YB) as fixed effect and the log10 transformed pre vaccination HI titer as covariate were fitted on log10 transformed post vaccination HI titer.

The following contrasts were performed:

- for both A strains (non-inferiority only): the GMT ratio of *Fluarix*, combining both TIV-YB and TIV-VB formulations, over FLU Q-QIV and the two-sided 95% CI;
- for the YB strain:
  - the GMT ratio of *Fluarix*-YB (TIV-YB) over FLU Q-QIV and the two-sided 95% CI to assess non-inferiority
  - the GMT ratio of FLU Q-QIV over *Fluarix*-VB (TIV-VB) and the two-sided 95% CI to assess superiority
- for the VB strain:
  - the GMT ratio of *Fluarix*-VB over FLU Q-QIV and the two-sided 95% CI to assess non-inferiority;
  - the GMT ratio of FLU Q-QIV over *Fluarix*-YB and the two-sided 95% CI to assess superiority.

The following evaluation criteria were considered:

Non-inferiority: the upper limit of two-sided 95% confidence interval on the GMT ratio (*Fluarix* over FLU Q-QIV) should not exceed 1.5.

Superiority: the lower limit of two-sided 95% confidence interval on the GMT ratio (FLU Q-QIV over *Fluarix*) ≥1.5.

Difference of SCRs:

For each strain, a logistic regression model including vaccine group (Q-QIV, TIV-VB, and TIV-YB) as fixed effect and the log10 transformed pre vaccination HI titer as covariate were fitted to the seroconversion response.

The following contrasts were performed:

- for both A strains (non-inferiority only): the SCR difference of *Fluarix*, combining both TIV-YB and TIV-VB formulations, with FLU Q-QIV and the two-sided 95% CI;
- for the YB strain:
  - the SCR difference of *Fluarix*-YB and FLU Q-QIV and the two-sided 95% CI to assess non-inferiority
  - the SCR difference of FLU Q-QIV and *Fluarix*-VB and the two-sided 95% CI to assess superiority
- for the VB strain:
  - the SCR difference of *Fluarix*-VB and FLU Q-QIV and the two-sided 95% CI to assess non-inferiority;
  - the SCR difference of FLU Q-QIV and *Fluarix*-YB and the two-sided 95% CI to assess superiority.

The following evaluation criteria were considered:

Non-inferiority: the upper limit of two-sided 95% confidence interval on the SCR difference (*Fluarix* minus FLU Q-QIV) should not exceed 10%.

Superiority: the lower limit of two-sided 95% confidence interval on the SCR difference (FLU Q-QIV minus *Fluarix*) should be ≥10%.

5.10.7.3. Exploratory analysis

For each of the influenza strains, the following parameters (with 95% confidence intervals) were calculated for each age group by pre-vaccination status:

- Geometric mean titers (GMT) of anti-HA antibody titers at Days 0 and 28
- Seroconversion Rates (SCR) at Day 28
- Seroprotection Rates (SPR) at Days 0 and 28.
- Seroconversion Factors (SCF) at Day 28

5.10.8. Analysis of safety

The primary analysis was based on the TVC. If the percent of vaccinated subjects excluded from the TVC was greater than 5%, a secondary (complementary) analysis was to be performed on the ATP-S cohort.

The percentages of subjects with at least one local adverse event (solicited and unsolicited), with at least one general adverse event (solicited and unsolicited) and with any adverse event during the solicited follow-up period were tabulated with exact 95% CI after each vaccine dose and overall. The percentages of doses followed by at least one local adverse event (solicited and unsolicited), by at least one general adverse event (solicited and unsolicited) and by any adverse event were tabulated in the same table.

The same tabulation was performed for grade 3 AEs, related AEs and grade 3 related AEs.

The percentages of subjects reporting each individual solicited local (any, grade 3 and medically attended) and general (any, grade 3, related, grade 3 related and medically attended) adverse event during the 7 day solicited follow-up period were tabulated with exact 95% CI. The percentage of doses followed by each individual solicited local and general adverse event was tabulated, with exact 95% CI.

The percentage of subjects with at least one report of unsolicited adverse event classified by the Medical Dictionary for Regulatory Activities (MedDRA) and reported up to 27 days after vaccination was tabulated with exact 95% CI. The same tabulation was performed for grade 3 unsolicited adverse events, for unsolicited adverse events with a relationship to vaccination and grade 3 unsolicited adverse events with relationship to vaccination.

The percentage of subjects reporting AEs resulting in a medically attended visit was also tabulated.

MAEs, SAEs and pIMDs were collected and summarized through the entire follow-up period. In addition, serious adverse events and withdrawal due to adverse events were described in detail.

The incidences of concomitant medication and vaccinations were tabulated.

5.10.9. Methodology for computing Confidence Intervals (CIs)

All Confidence Intervals (CI) were 2-sided 95% CI.

The exact 95% CIs for a proportion within a group was calculated using Proc StatXact software.

The 95% CI for geometric mean titers/concentrations (GMTs/GMCs) was obtained within each group separately. The 95% CI for the mean of log-transformed titer/ was first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs was then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titer.

5.10.10. Sequence of analyses

A single analysis was conducted when both active phase data through Day 56 and extended safety follow-up data through Day 180 were available and cleaned.

5.10.11. Interim analysis

No interim analysis was planned or performed for this study.

5.11. Changes in the conduct of the study or planned analyses

5.11.1. Protocol amendments

There were no protocol amendments.

5.11.2. Other changes

The proportion of subjects with prior influenza vaccination was tabulated as ‘Yes’ or ‘No’ and was not tabulated as the 3 categories specified in the protocol.

6. STUDY POPULATION RESULTS

The following group names were used for the statistical analyses:

Group label/name in tables	Group definition
QIV1	FLU Q-QIV (3 - 17 year old subjects)
TIV-VB	*Fluarix* TIV Victoria B strain (3 - 17 year old subjects)
TIV-YB	*Fluarix* TIV Yamagata B strain (3 - 17 year old subjects)
QIV2	FLU Q-QIV (6 - 35 months old subjects)

6.1. Study dates

The first subject was enrolled in the study on 01 October 2010 and the last study visit (last subject, last visit) occurred on 06 July 2011.

6.2. Subject eligibility and attrition from the study

6.2.1. Number of subjects

The target sample size for the study was 3000 subjects including 2700 subjects 3 to 17 years of age and 300 subjects 6 to 35 months old. The actual total number enrolled in the study was 3109 subjects, of which 3094 subjects were vaccinated (i.e., the Total Vaccinated Cohort or TVC): 932 in the QIV1 group, 929 in the TIV-VB group, 932 in the TIV-YB group, all 3 to 17 years of age, and 301 in the QIV2 group (6 to 35 months old) (Table 16). The number and distribution of vaccinated subjects across the 32 study centers are described in Supplement 1.

6.2.2. Study completion and withdrawal from study

The number of subjects vaccinated, completed, withdrawn, and the reasons for withdrawal are summarized (Table 16). Of the 134 total subject withdrawals by the end of the study, none were due to a serious adverse event (SAE), and only one withdrawal (in the QIV2 group) was due to a non-serious adverse event (AE). The majority of the withdrawals occurred because the subjects were lost to follow-up or due to consent withdrawals unrelated to an AE.

Table 16 Number of subjects vaccinated, completed, and withdrawn with reason for withdrawal (TVC)

	QIV1	TIV-VB	TIV-YB	QIV2	Total
Number of subjects vaccinated	932	929	932	301	3094
Number of subjects completed	894	889	902	275	2960
Number of subjects withdrawn	38	40	30	26	134
Reasons for withdrawal :					
Serious Adverse Event	0	0	0	0	0
Non-Serious Adverse Event	0	0	0	1	1
Protocol violation	0	0	0	2	2
Consent withdrawal (not due to an adverse event)	9	4	7	5	25
Migrated/moved from study area	0	0	0	4	4
Lost to follow-up (subjects with incomplete vaccination course)	3	6	3	2	14
Lost to follow-up (subjects with complete vaccination course)	25	30	19	12	86
Sponsor study termination	0	0	0	0	0
Other - client unable to come to center within window period	0	0	1	0	1
Other - pi decision due to excessive no-shows	1	0	0	0	1

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last visit

Additional data on the number of subjects at each visit and lists of the subjects who were withdrawn from the study are provided in Supplement 2.

6.2.3. Protocol deviations

The total number of subjects enrolled, the number of subjects eligible for the different according-to-protocol (ATP) analyses, and reasons for elimination are provided in Table 17. Subjects were eliminated from the ATP cohorts based on the lowest elimination code, as more than one elimination code could be assigned to the same subject. Following elimination of subjects from the total enrolled cohort, the Total Vaccinated Cohort (TVC), ATP cohort for safety (ATP-S), and ATP cohort for immunogenicity (ATP-I) cohorts consisted of 3094, 3071, and 2886 subjects, respectively.

Fifteen subjects were not vaccinated and, therefore, not included in the TVC. Twenty-three subjects were eliminated from the TVC (n=3094) to generate the ATP-S (n=3071) (Table 17). Since the number of eliminated subjects represented less than 5% of the TVC, the analysis of safety was not performed on the ATP-S and was based only on the TVC (the primary cohort for analysis of safety).

A total of 208 subjects (including the 23 mentioned above) were eliminated from the TVC (n=3094) to generate the ATP-I (n=2886) (Table 17). The primary reason for exclusion was non-compliance with blood sampling schedule (38 subjects) and essential serological data missing (127 subjects). Since the number of eliminated subjects represented more than 5% of the TVC, the analysis of immunogenicity was performed on

both the ATP-I (primary analysis) and the TVC (complementary analysis), to ensure that no bias was introduced into the ATP-I analysis as a result of subject elimination.

The randomization code was broken and treatment assignment revealed at the investigator site for only one subject, due to a randomization error (PID (b) (6) in the TIV-VB group).

The number of deviations for age and interval between study visits for subjects (3-17 years of age) are summarized in Supplement 3 (primed subjects) and Supplement 4 (unprimed subjects). The number of deviations for age and interval between study visits for subjects (6-35 months of age in the QIV2 group only) are summarized in Supplement 5 and Supplement 6 for primed and unprimed subjects, respectively.

Table 17 Number of subjects enrolled in the study and number of subjects excluded from ATP analyses with reasons for exclusion

	Total			QIV1		TIV-VB		TIV-YB		QIV2		NOGRP	
Title	**n**	**s**	**%**	**n**	**s**	**n**	**s**	**n**	**s**	**n**	**s**	**n**	**s**
Total cohort	**3109**			**932**		**929**		**932**		**302**		**14**	
Study vaccine dose not administrated but subject number allocated (code 1030)	15	15		0	0	0	0	0	0	1	1	14	14
Total vaccinated cohort (TVC)	**3094**		**100**	**932**		**929**		**932**		**301**		**0**	
Administration of vaccine(s) forbidden in the protocol (code 1040)	12	12		5	5	2	2	2	2	3	3	0	0
Randomisation code broken at the investigator site (code 1060)	1	1		0	0	1	1	0	0	0	0	0	0
Study vaccine dose not administered according to protocol (code 1070)	10	11		3	4	2	2	4	4	1	1	0	0
ATP cohort for safety (ATP-S)	**3071**		**99.3**	**924**		**924**		**926**		**297**		**0**	
Protocol violation (inclusion/exclusion criteria) (code 2010)	1	1		0	0	0	0	0	0	1	1	0	0
Non compliance with vaccination schedule (including wrong and unknown dates) (code 2080)	19	19		3	3	7	7	4	4	5	5	0	0
Non compliance with blood sampling schedule (including wrong and unknown dates (code 2090)	38	40		7	7	11	11	12	12	8	10	0	0
Essential serological data missing (code 2100)	127	154		36	43	35	38	32	34	24	25	0	14
ATP cohort for immunogenicity (ATP-I)	**2886**		**93.3**	**878**		**871**		**878**		**259**		**0**	

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
NOGRP = No assigned group
Note: Subjects may have more than one elimination code assigned
n = number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
s = number of subjects with the elimination code assigned
% = percentage of subjects in the considered ATP cohort relative to the Total vaccinated cohort

6.3. Demographic characteristics

6.3.1. ATP cohort for analysis of Immunogenicity (ATP-I) and Total Vaccinated Cohort (TVC)

The primary analysis of immunogenicity was based on the ATP-I. Since the percent of vaccinated subjects excluded from this ATP cohort was more than 5% of the TVC, a second analysis based on the TVC was performed to complement the ATP-I analysis. Consequently, demographic characteristics of both the ATP -I (Table 18) and the TVC (Table 19) are presented.

The demographic profile of the three treatment groups of subjects in the ATP-I cohort at the time of first vaccination was comparable with respect to mean age, gender, and ethnicity/geographic ancestry distribution (Table 18). Overall, the mean age was 9 years and the population was predominantly of White-Caucasian/European heritage (62.6%), with 51.5% male subjects. The demographic characteristics of the TVC (Table 19) were very similar to those of the ATP-I.

Summaries of demographic characteristics of the QIV2 group (6-35 months old) are presented in Table 20 (ATP-I) and Table 21 (TVC). The mean age (ATP-I) was 1.3 years (16 months) and the population was also predominantly of White-Caucasian/European heritage (71.0%), with 52.1% male subjects. The TVC demographic characteristics for the QIV2 group were similar to those of the ATP-I.

The history of influenza vaccination in the previous three seasons (TVC) is presented in Supplement 7.

Table 18 Summary of demographic characteristics (3-17 years of age) (ATP-I)

		QIV1 N = 878		TIV-VB N = 871		TIV-YB N = 878		Total N = 2627	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (years) at vaccination dose: 1	Mean	9.0	-	9.0	-	9.0	-	9.0	-
	SD	4.24	-	4.24	-	4.17	-	4.22	-
	Median	9.0	-	9.0	-	9.0	-	9.0	-
	Minimum	3	-	3	-	3	-	3	-
	Maximum	17	-	17	-	17	-	17	-
Age (months) at vaccination dose: 1	Mean	114.0	-	113.0	-	113.0	-	113.4	-
	SD	51.34	-	51.25	-	50.18	-	50.91	-
	Median	110.0	-	110.0	-	112.0	-	110.0	-
	Minimum	36	-	36	-	36	-	36	-
	Maximum	215	-	215	-	215	-	215	-
Gender	Female	406	46.2	428	49.1	441	50.2	1275	48.5
	Male	472	53.8	443	50.9	437	49.8	1352	51.5
Ethnicity	American hispanic or latino	224	25.5	220	25.3	228	26.0	672	25.6
	Not american hispanic or latino	654	74.5	651	74.7	650	74.0	1955	74.4
Geographic Ancestry	African heritage / african american	74	8.4	80	9.2	83	9.5	237	9.0
	American indian or alaskan native	4	0.5	0	0.0	1	0.1	5	0.2
	Asian - central/south asian heritage	13	1.5	16	1.8	21	2.4	50	1.9
	Asian - east asian heritage	97	11.0	100	11.5	95	10.8	292	11.1
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	3	0.3	5	0.6	4	0.5	12	0.5
	Native hawaiian or other pacific islander	3	0.3	1	0.1	4	0.5	8	0.3
	White - arabic / north african heritage	3	0.3	7	0.8	6	0.7	16	0.6
	White - caucasian / european heritage	565	64.4	539	61.9	540	61.5	1644	62.6
	Other	116	13.2	123	14.1	124	14.1	363	13.8

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 19 Summary of demographic characteristics (3-17 years of age) (TVC)

		QIV1 N = 932		TIV-VB N = 929		TIV-YB N = 932		Total N = 2793	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (years) at vaccination dose: 1	Mean	8.9	-	8.9	-	8.9	-	8.9	-
	SD	4.21	-	4.23	-	4.17	-	4.20	-
	Median	8.0	-	9.0	-	9.0	-	9.0	-
	Minimum	3	-	2	-	3	-	2	-
	Maximum	17	-	17	-	17	-	17	-
Age (months) at vaccination dose: 1	Mean	112.4	-	111.8	-	111.8	-	112.0	-
	SD	51.06	-	51.10	-	50.08	-	50.73	-
	Median	107.0	-	108.0	-	108.5	-	108.0	-
	Minimum	36	-	34	-	36	-	34	-
	Maximum	215	-	215	-	215	-	215	-
Gender	Female	434	46.6	455	49.0	464	49.8	1353	48.4
	Male	498	53.4	474	51.0	468	50.2	1440	51.6
Ethnicity	American hispanic or latino	235	25.2	235	25.3	245	26.3	715	25.6
	Not american hispanic or latino	697	74.8	694	74.7	687	73.7	2078	74.4
Geographic Ancestry	African heritage / african american	83	8.9	85	9.1	87	9.3	255	9.1
	American indian or alaskan native	6	0.6	1	0.1	1	0.1	8	0.3
	Asian - central/south asian heritage	17	1.8	19	2.0	23	2.5	59	2.1
	Asian - east asian heritage	98	10.5	100	10.8	98	10.5	296	10.6
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	4	0.4	6	0.6	4	0.4	14	0.5
	Native hawaiian or other pacific islander	3	0.3	1	0.1	4	0.4	8	0.3
	White - arabic / north african heritage	3	0.3	7	0.8	7	0.8	17	0.6
	White - caucasian / european heritage	598	64.2	580	62.4	575	61.7	1753	62.8
	Other	120	12.9	130	14.0	133	14.3	383	13.7

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 20 Summary of demographic characteristics for QIV2 group (6-35 months of age) (ATP-I)

		QIV2 N = 259		Total N = 259	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**
Age (years) at vaccination dose: 1	Mean	1.3	-	1.3	-
	SD	0.72	-	0.72	-
	Median	1.0	-	1.0	-
	Minimum	0	-	0	-
	Maximum	2	-	2	-
Age (months) at vaccination dose: 1	Mean	21.3	-	21.3	-
	SD	8.58	-	8.58	-
	Median	21.0	-	21.0	-
	Minimum	6	-	6	-
	Maximum	35	-	35	-
Gender	Female	124	47.9	124	47.9
	Male	135	52.1	135	52.1
Ethnicity	American hispanic or latino	48	18.5	48	18.5
	Not american hispanic or latino	211	81.5	211	81.5
Geographic Ancestry	African heritage / african american	38	14.7	38	14.7
	American indian or alaskan native	6	2.3	6	2.3
	Asian - central/south asian heritage	9	3.5	9	3.5
	Asian - east asian heritage	1	0.4	1	0.4
	Asian - japanese heritage	0	0.0	0	0.0
	Asian - south east asian heritage	2	0.8	2	0.8
	Native hawaiian or other pacific islander	0	0.0	0	0.0
	White - arabic / north african heritage	7	2.7	7	2.7
	White - caucasian / european heritage	184	71.0	184	71.0
	Other	12	4.6	12	4.6

QIV2 = Flu Q-QIV (6 - 35 months)
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 21 Summary of demographic characteristics for QIV2 group (6-35 months of age) (TVC)

		QIV2 N = 301		Total N = 301	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**
Age (years) at vaccination dose: 1	Mean	1.2	-	1.2	-
	SD	0.73	-	0.73	-
	Median	1.0	-	1.0	-
	Minimum	0	-	0	-
	Maximum	2	-	2	-
Age (months) at vaccination dose: 1	Mean	21.0	-	21.0	-
	SD	8.68	-	8.68	-
	Median	21.0	-	21.0	-
	Minimum	6	-	6	-
	Maximum	35	-	35	-
Gender	Female	143	47.5	143	47.5
	Male	158	52.5	158	52.5
Ethnicity	American hispanic or latino	56	18.6	56	18.6
	Not american hispanic or latino	245	81.4	245	81.4
Geographic Ancestry	African heritage / african american	48	15.9	48	15.9
	American indian or alaskan native	6	2.0	6	2.0
	Asian - central/south asian heritage	13	4.3	13	4.3
	Asian - east asian heritage	2	0.7	2	0.7
	Asian - japanese heritage	0	0.0	0	0.0
	Asian - south east asian heritage	3	1.0	3	1.0
	Native hawaiian or other pacific islander	0	0.0	0	0.0
	White - arabic / north african heritage	7	2.3	7	2.3
	White - caucasian / european heritage	206	68.4	206	68.4
	Other	16	5.3	16	5.3

QIV2 = Flu Q-QIV (6 - 35 months)
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

7. IMMUNOGENICITY RESULTS

The following group names were used for the statistical analyses:

Group label/name in tables	Group definition
QIV1	FLU Q-QIV (3 - 17 year old subjects)
TIV-VB	*Fluarix* TIV Victoria B strain (3 - 17 year old subjects)
TIV-YB	*Fluarix* TIV Yamagata B strain (3 - 17 year old subjects)
QIV2	FLU Q-QIV (6 - 35 months old subjects)

7.1. Data sets analyzed

The primary analysis of immunogenicity was performed on the ATP cohort for immunogenicity (ATP-I). Since the percentage of vaccinated subjects excluded from this ATP cohort was more than 5%, a second analysis based on the Total vaccinated cohort was performed to complement the ATP analysis. See Section 5.10.4 for the definition of the cohorts identified for analyses and Section 6.2 for eligibility for analyses.

7.2. According-to-protocol analysis of cohort for immunogenicity (ATP-I)

7.2.1. Primary objective

7.2.1.1. Immunogenic non-inferiority of FLU Q-QIV versus *Fluarix*-VB (TIV-VB) or *Fluarix*-YB (TIV-YB) with respect to the A and B strains common to Q-QIV and either TIV (in 3 to 17 year old subjects)

The adjusted GMT ratios (with 95% CIs) are shown in Table 22 through Table 24and differences in SCRs (with 95% CIs) are shown in Table 25 through Table 27 for all four vaccine strains in FLU Q-QIV.

The results indicated that the pre-defined statistical criteria required for demonstration of immunogenic non-inferiority of FLU Q-QIV versus *Fluarix*-VB and *Fluarix*-YB with respect to the A and B strains common to Q-QIV and either TIV, in children 3 years to 17 years of age, were met for each FLU Q-QIV influenza vaccine strain (FDA/CBER's non-inferiority criteria: upper limit (UL) of the two-sided 95 % CI (confidence interval) of the adjusted GMT ratio ≤ 1.5 *and* UL of the two-sided 95 % CI of the difference in SCR ≤ 10% for all vaccine strains).

For adjusted GMT Ratios:

- The UL of the two sided 95% CI for the adjusted GMT ratio of TIV (pooled TIV *Fluarix*-VB and *Fluarix*-YB) over Q-QIV was **1.25** for the A/California/7/2009 (H1N1) strain and **1.07** for the A/Victoria/210/2009 (H3N2) strain, which did not exceed 1.5;
- The UL of the two sided 95% CI for the adjusted GMT ratio for *Fluarix*-VB over Q-QIV for the B/Brisbane/60/2008 (Victoria lineage) strain was **1.07**, which did not exceed 1.5;

- The UL of two sides 95% CI for the adjusted GMT ratio for *Fluarix*-YB over Q-QIV for the B/Florida/4/2006 (Yamagata lineage) strain was **1.16**, which did not exceed 1.5.

For the difference in SCR:

- The UL of the two sided 95% CI for the difference in SCR of TIV (pooled TIV *Fluarix*-VB and *Fluarix*-YB) minus Q-QIV was **4.77%** for the A/California/7/2009 (H1N1) strain and **2.41%** for theA/Victoria/210/2009 (H3N2) strain, which did not exceed 10%;
- The UL of the two sided 95% CI for the difference in SCR for *Fluarix*-VB minus Q-QIV for the B/Brisbane/60/2008 (Victoria lineage) strain was **1.12%**, which did not exceed 10%;
- The UL of the two sided 95% CI for the difference in SCR for *Fluarix*-YB minus Q-QIV for the B/Florida/4/2006 (Yamagata lineage) strain was **2.30%**, which did not exceed 10%.

Table 22 Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) and *Fluarix*-YB (TIV-YB) in terms of adjusted GMT ratios of HI antibody post-last vaccination for the A/California/7/2009 (H1N1) and A/Victoria/210/2009 (H3N2) strains (ATP-I)

					Adjusted GMT ratio (TIV-VB+TIV-YB / QIV1)		
	TIV-VB+TIV-YB		QIV1			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
A/California/7/2009 (H1N1)	1747	421.4	876	366.3	1.15	1.06	1.25
A/Victoria/210/2009 (H3N2)	1746	144.3	876	145.8	0.99	0.92	1.07

TIV-VB+TIV-YB = Pooled TIV Fluarix-VB and Fluarix-YB groups (3 - 17 years)
QIV1 = Flu Q-QIV (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Table 23 Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) in terms of adjusted GMT ratios of HI antibody post-last vaccination for the B/Brisbane/60/2008 (Victoria) strain (ATP-I)

					Adjusted GMT ratio (TIV-VB / QIV1)		
	TIV-VB		QIV1			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
B/Brisbane/60/2008 (Victoria)	870	243.4	876	252.5	0.96	0.87	1.07

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Table 24 Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-YB (TIV-YB) in terms of adjusted GMT ratios of HI antibody post-last vaccination for the B/Florida/4/2006 (Yamagata) strain (ATP-I)

					Adjusted GMT ratio (TIV-YB / QIV1)		
	TIV-YB		QIV1			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
B/Florida/4/2006 (Yamagata)	877	564.6	876	525.2	1.08	0.99	1.16

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Table 25 Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) and *Fluarix*-YB (TIV-YB) in terms of seroconversion rate (difference in seroconversion rate) at day 28 for the A/California/7/2009 (H1N1) and A/Victoria/210/2009 (H3N2) strains (ATP-I)

							Difference in seroconversion rate (TIV-VB+TIV-YB minus QIV1)		
	QIV1			TIV-VB+TIV-YB				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
A/California/7/2009 (H1N1) (1/DIL)	876	739	84.4	1747	1505	86.1	1.79	-1.04	4.77
A/Victoria/210/2009 (H3N2) (1/DIL)	876	614	70.1	1746	1200	68.7	-1.36	-5.05	2.41

TIV-VB+TIV-YB = Pooled TIV groups (3 - 17 years)
QIV1 = Flu Q-QIV (3 - 17 years)
Seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
Seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 26 Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) and *Fluarix*-YB (TIV-YB) in terms of seroconversion rate (difference in seroconversion rate) at day 28 for the B/Brisbane/60/2008 (Victoria) strain (ATP-I)

							Difference in seroconversion rate (TIV-VB minus QIV1)		
	QIV1			TIV-VB+TIV-YB				95% CI	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
B/Brisbane/60/2008 (Victoria) (1/DIL)	876	653	74.5	870	622	71.5	-3.05	-7.21	1.12

TIV-VB+TIV-YB = Pooled TIV groups (3 - 17 years)
QIV1 = Flu Q-QIV (3 - 17 years)
Seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
Seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 27 Non-inferiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) and *Fluarix*-YB (TIV-YB) in terms of seroconversion rate (difference in seroconversion rate) at day 28 for the B/Florida/4/2006 (Yamagata) strain (ATP-I)

							Difference in seroconversion rate (TIV-YB minus QIV1)		
	QIV1			TIV-VB+TIV-YB				95% CI	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
B/Florida/4/2006 (Yamagata) (1/DIL)	876	659	75.2	877	644	73.4	-1.80	-5.89	2.30

TIV-VB+TIV-YB = Pooled TIV groups
QIV1 = Flu Q-QIV (3 - 17 years)
Seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
Seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

7.2.2. Secondary objectives:

7.2.2.1. Immunogenic superiority (in 3 to 17 year old subjects) of FLU Q-QIV versus *Fluarix*-VB or *Fluarix*-YB with respect to the B strains in Q-QIV not shared with either TIV

The adjusted GMT ratios (with 95% CIs) are shown in Table 28 (for the B/Florida/4/2006 Yamagata strain B) and in Table 29 (for the Victoria strain B). The differences in SCRs (with 95% CIs) are presented in Table 30 (for the B/Florida/4/2006 Yamagata strain B) and Table 31 (for the B/Brisbane/60/2008 Victoria strain B).

The results indicated that the pre-defined statistical criteria required for demonstration of immunogenic superiority of the FLU Q-QIV versus *Fluarix*-VB and *Fluarix*-YB, in 3 to 17 year old children, with respect to the B strains present in Q-QIV but absent from either TIV, were met (superiority criteria: lower limit of the two-sided 95 % CI of the adjusted GMT ratio > 1.5 *and* lower limit of the two-sided 95 % CI of the difference in SCR > 10%).

For adjusted GMT Ratios:

- The LL of the two sided 95% CI for the GMT ratio of Q-QIV over *Fluarix*-VB for the B/Florida/4/2006 (Yamagata lineage) strain was **2.41**, which was greater than 1.5;
- The LL of the two sided 95% CI for the GMT ratio for Q-QIV over *Fluarix*-YB for the B/Brisbane/60/2008 (Victoria lineage) strain was **3.43**, which was greater than 1.5.

For the difference in SCR:

- The LL of the two sided 95% CI for the difference in SCR of Q-QIV minus *Fluarix*-VB for the B/Florida/4/2006 (Yamagata lineage) strain was **29.55%**, which was greater than 10%;
- The LL of the two sided 95% CI for the difference in SCR of Q-QIV minus *Fluarix*-YB for the B/Brisbane/60/2008 (Victoria lineage) strain was **40.35%**, which was greater than 10%.

Table 28 Superiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) in terms of adjusted GMT ratios of HI antibody post-last vaccination for the B/Florida/4/2006 (Yamagata) strain (ATP-I)

					Adjusted GMT ratio (QIV1 / TIV-VB)		
	QIV1		TIV-VB			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
B/Florida/4/2006 (Yamagata)	876	513.8	870	196.5	2.61	2.41	2.84

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Table 29 Superiority of FLU Q-QIV (QIV1) versus *Fluarix*-YB (TIV-YB) in terms of adjusted GMT ratios of HI antibody post-last vaccination for the B/Brisbane/60/2008 (Victoria) strain (ATP-I)

					Adjusted GMT ratio (QIV1 / TIV-YB)		
	QIV1		TIV-YB			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
B/Brisbane/60/2008 (Victoria)	876	253.7	876	67.2	3.78	3.43	4.16

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Table 30 Superiority of FLU Q-QIV (QIV1) versus *Fluarix*-VB (TIV-VB) in terms of seroconversion rate (difference in seroconversion rate) at day 28 for the B/Florida/4/2006 (Yamagata) strain (ATP-I)

							Difference in vaccine response rate (QIV1 minus TIV-VB)		
	QIV1			TIV-VB				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
B/Florida/4/2006 (Yamagata) (1/DIL)	876	659	75.2	870	359	41.3	33.96	29.55	38.24

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
Seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
Seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 31 Superiority of FLU Q-QIV (QIV1) versus *Fluarix*-YB (TIV-YB) in terms of seroconversion rate (difference in seroconversion rate) at day 28 for the the B/Brisbane/60/2008 (Victoria) strain (ATP-I)

							Difference in vaccine response rate (QIV1 minus TIV-YB)		
	QIV1			TIV-YB				95% CI	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
B/Brisbane/60/2008 (Victoria) (1/DIL)	876	653	74.5	876	262	29.9	44.63	40.35	48.72

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
Seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

7.2.2.2. Descriptive immunogenicity (overall) of FLU Q-QIV, *Fluarix*-VB, and *Fluarix*-YB in terms of GMT, SCR, SPR, and SCF

7.2.2.2.1. Analysis of GMTs for HI antibody titers (ATP-I)

Point estimates for the GMTs are described below:

For subjects 3 to 17 years old:

- The post vaccination GMTs for the A/California/7/2009 (H1N1) had point estimates of: 362.7 for QIV1, 429.1 for TIV-VB and 420.2 for TIV-YB.
- The post vaccination GMTs for the A/Victoria/210/2009 (H3N2) reached a point estimate of: 143.7 for Q-QIV, 139.6 for TIV-VB and 151 for TIV-YB.
  - The post vaccination GMTs for the B/Brisbane/60/2008 (Victoria lineage) reached a point estimate of: 250.5 for Q-QIV, 245.4 for TIV-VB and 68.1 for TIV-YB (TIV-YB did not contain B/Brisbane/60/2008, Victoria lineage, strain).
  - The post vaccination GMTs for the B/Florida/4/2006 (Yamagata lineage) reached a point estimate of: 512.5 for Q-QIV, 579 for TIV-YB, and 197 for TIV-VB (TIV-VB did not contain B/Florida/4/2006, Yamagata lineage, strain).

For subjects 6 to 35 months old receiving FLU Q-QIV only (QIV2 group):

The post vaccination GMTs reached a point estimate of 200.9 for the A/California/7/2009 (H1N1), 61.4 for the A/Victoria/210/2009 (H3N2), 127.3 for the B/Brisbane/60/2008 (Victoria) and 192.7 for the B/Florida/4/2006 (Yamagata).

Table 32 Seropositivity rates and GMTs for HI antibody titers at Day 0 and at 28 days following last vaccination (ATP-I)

				≥ 10 1/DIL				GMT		
						95% CI			95% CI	
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)	QIV1	PRE	876	629	71.8	68.7	74.8	29.4	26.8	32.2
		POST	878	871	99.2	98.4	99.7	362.7	335.3	392.3
	TIV-VB	PRE	870	641	73.7	70.6	76.6	32.2	29.4	35.3
		POST	871	865	99.3	98.5	99.7	429.1	396.5	464.3
	TIV-YB	PRE	877	639	72.9	69.8	75.8	29.1	26.6	31.8
		POST	878	876	99.8	99.2	100	420.2	388.8	454.0
	QIV2	PRE	259	116	44.8	38.6	51.1	16.8	13.9	20.3
		POST	259	255	98.5	96.1	99.6	200.9	166.6	242.2
A/Victoria/210/2009 (H3N2)	QIV1	PRE	876	566	64.6	61.3	67.8	18.1	16.7	19.7
		POST	878	872	99.3	98.5	99.7	143.7	134.2	153.9
	TIV-VB	PRE	870	578	66.4	63.2	69.6	19.0	17.4	20.6
		POST	871	862	99.0	98.0	99.5	139.6	130.5	149.3
	TIV-YB	PRE	876	568	64.8	61.6	68.0	19.4	17.8	21.1
		POST	878	871	99.2	98.4	99.7	151.0	141.0	161.6
	QIV2	PRE	259	18	6.9	4.2	10.8	5.6	5.3	6.0
		POST	259	252	97.3	94.5	98.9	61.4	53.8	70.0
B/Brisbane/60/2008 (Victoria)	QIV1	PRE	876	587	67.0	63.8	70.1	24.8	22.5	27.3
		POST	878	871	99.2	98.4	99.7	250.5	230.8	272.0
	TIV-VB	PRE	870	597	68.6	65.4	71.7	25.8	23.5	28.4
		POST	871	862	99.0	98.0	99.5	245.4	226.9	265.4
	TIV-YB	PRE	877	611	69.7	66.5	72.7	25.8	23.5	28.4
		POST	877	792	90.3	88.2	92.2	68.1	61.9	74.9
	QIV2	PRE	259	76	29.3	23.9	35.3	8.7	7.5	10.0
		POST	259	255	98.5	96.1	99.6	127.3	109.4	148.1
B/Florida/4/2006 (Yamagata)	QIV1	PRE	876	715	81.6	78.9	84.1	57.9	52.0	64.4
		POST	878	877	99.9	99.4	100	512.5	477.6	549.9
	TIV-VB	PRE	870	717	82.4	79.7	84.9	58.4	52.6	64.9
		POST	871	856	98.3	97.2	99.0	197.0	180.7	214.8
	TIV-YB	PRE	877	725	82.7	80.0	85.1	65.9	59.3	73.2
		POST	878	877	99.9	99.4	100	579.0	541.2	619.3
	QIV2	PRE	259	69	26.6	21.4	32.5	7.7	7.0	8.6
		POST	259	258	99.6	97.9	100	192.7	172.1	215.7

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST= Day 28 post last vaccination

7.2.2.2.2. Analysis of Seroconversion rates (ATP-I)

The seroconversion rates (SCRs), i.e., either a pre-vaccination HI titer <10 and a post-vaccination titer ≥40, or a pre-vaccination titer ≥10 and a minimum four-fold increase post-vaccination, are shown for all subjects in Table 33 and by age groups in Supplement 21.

Point estimates for the SCRs are described below:

For subjects 3 to 17 years old:

- The post vaccination SCRs for the A/California/7/2009 (H1N1) reached a point estimate of: 84.4% for QIV1, 86.8% for TIV-VB and 85.5% for TIV-YB.
- The post vaccination SCRs for the A/Victoria/210/2009 (H3N2) reached a point estimate of: 70.1% for Q-QIV, 67.8% for TIV-VB and 69.6% for TIV-YB.
- The post vaccination SCRs for the B/Brisbane/60/2008 (Victoria lineage) reached a point estimate of: 74.5% for Q-QIV, 71.5% for TIV-VB and 29.9% for TIV-YB (TIV-YB did not contain B/Brisbane/60/2008, Victoria lineage, strain).
- The post vaccination SCRs for the B/Florida/4/2006 (Yamagata lineage) reached a point estimate of: 75.2% for Q-QIV, 73.4% for TIV-YB, and 41.3% for TIV-VB (TIV-VB did not contain B/Florida/4/2006, Yamagata lineage, strain.

For all strains included in the QIV, TIV-VB, and TIV-YB vaccines, in subjects 3 to 17 years of age, the lower limit (LL) of the 95% CI for SCR exceeded 40%, an immunogenicity criterion predictive of clinical benefit (FDA/CBER criterion of vaccine immunogenicity for adults <65 years of age and for the pediatric population) [FDA, 2007].

For subjects 6 to 35 months old receiving FLU Q-QIV only (QIV2 group):

The post vaccination SCRs reached a point estimate of 84.9% for the A/California/7/2009 (H1N1), 73% for the A/Victoria/210/2009 (H3N2), 84.6% for the B/Brisbane/60/2008 (Victoria) and 93.8% for the B/Florida/4/2006 (Yamagata) strains (Table 33).

For all strains included in the QIV, in subjects 6 to 35 months of age, the lower limit (LL) of the 95% CI for SCR exceeded 40%, an immunogenicity criterion predictive of clinical benefit (FDA/CBER criterion of vaccine immunogenicity for adults <65 years of age and for the pediatric population) [FDA, 2007].

Table 33 Seroconversion rate (SCR) for HI antibody titers at 28 days following last vaccination (ATP-I)

			SCR			
					95% CI	
Strain	Group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	876	739	84.4	81.8	86.7
	TIV-VB	870	755	86.8	84.3	89.0
	TIV-YB	877	750	85.5	83.0	87.8
	QIV2	259	220	84.9	80.0	89.1
A/Victoria/210/2009 (H3N2)	QIV1	876	614	70.1	66.9	73.1
	TIV-VB	870	590	67.8	64.6	70.9
	TIV-YB	876	610	69.6	66.5	72.7
	QIV2	259	189	73.0	67.1	78.3
B/Brisbane/60/2008 (Victoria)	QIV1	876	653	74.5	71.5	77.4
	TIV-VB	870	622	71.5	68.4	74.5
	TIV-YB	876	262	29.9	26.9	33.1
	QIV2	259	219	84.6	79.6	88.7
B/Florida/4/2006 (Yamagata)	QIV1	876	659	75.2	72.2	78.1
	TIV-VB	870	359	41.3	38.0	44.6
	TIV-YB	877	644	73.4	70.4	76.3
	QIV2	259	243	93.8	90.2	96.4

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4-fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST= Day 28 post last vaccination

7.2.2.2.3. Analysis of Seroprotection rates (ATP-I)

The seroprotection rates (SPRs), i.e., the percentages of vaccinees with a serum HI titer ≥ 1:40 with 95% CI, are shown in Table 34 for all subjects overall and in Supplement 22 by age groups.

For subjects 3 to 17 years old:

- The post vaccination SPRs for the A/California/7/2009 (H1N1) strain reached a point estimate of: 96.8% , 97.4, 96.6 for the Q-QIV, TIV-VB, and TIV-YB groups, respectively.
- The post vaccination SPRs for the A/Victoria/210/2009 (H3N2) reached a point estimate of: 92.9%, 92.8, and 93.3 for the Q-QIV, TIV-VB, and TIV-YB groups, respectively.
- The post vaccination SPRs for the B/Brisbane/60/2008 (Victoria lineage) reached a point estimate of: 95.4% for Q-QIV, 96.3% for TIV-VB, and 73.3% for TIV-YB (TIV-YB did not contain the B/Brisbane/60/2008, Victoria lineage, strain).

- The post vaccination SPRs for the B/Florida/4/2006 (Yamagata lineage) reached a point estimate of: 99% for Q-QIV, 99.4% for TIV-YB and 92.4% for TIV-VB (TIV-VB did not contain the B/Florida/4/2006, Yamagata lineage, strain).
- For each shared strain between Q-QIV and TIV-VB or TIV-YB, in subjects 3-17 years of age, the lower limit (LL) of the 95% CI for SPR exceeded 70%, an immunogenicity criterion predictive of clinical benefit (FDA/CBER criterion of vaccine immunogenicity for adults <65 years of age and for the pediatric population) [FDA, 2007].

For subjects 6 to 35 months old receiving FLU Q-QIV only (QIV2 group):

- The post vaccination SPRs reached a point estimate of 89.6% for the A/California/7/2009 (H1N1), 74.5% for the A/Victoria/210/2009 (H3N2), 88% for the B/Brisbane/60/2008 (Victoria lineage) and 96.5% for the B/Brisbane/3/2007 (Yamagata lineage) strains (Table 34).

For all strains included in QIV in subjects 6-35 months of age, the lower limit (LL) of the 95% CI for SPR exceeded 70%, an immunogenicity criterion predictive of clinical benefit (FDA/CBER criterion of vaccine immunogenicity for adults <65 years of age and for the pediatric population) [FDA, 2007] except for the A/Victoria/210/2009 (H3N2) strain (LL of 95% CI of SPR=68.8%)..

Table 34 Seroprotection rates (SPR) for HI antibody titers at Day 0 and at 28 days following last vaccination (ATP-I)

				SPR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	PRE	876	480	54.8	51.4	58.1
		POST	878	850	96.8	95.4	97.9
	TIV-VB	PRE	870	496	57.0	53.6	60.3
		POST	871	848	97.4	96.1	98.3
	TIV-YB	PRE	877	477	54.4	51.0	57.7
		POST	878	848	96.6	95.2	97.7
	QIV2	PRE	259	87	33.6	27.9	39.7
		POST	259	232	89.6	85.2	93.0
A/Victoria/210/2009 (H3N2)	QIV1	PRE	876	295	33.7	30.5	36.9
		POST	878	816	92.9	91.0	94.5
	TIV-VB	PRE	870	301	34.6	31.4	37.9
		POST	871	808	92.8	90.8	94.4
	TIV-YB	PRE	876	324	37.0	33.8	40.3
		POST	878	819	93.3	91.4	94.8
	QIV2	PRE	259	7	2.70	1.1	5.5
		POST	259	193	74.5	68.8	79.7
B/Brisbane/60/2008 (Victoria)	QIV1	PRE	876	388	44.3	41.0	47.7
		POST	878	838	95.4	93.8	96.7
	TIV-VB	PRE	870	404	46.4	43.1	49.8
		POST	871	839	96.3	94.9	97.5
	TIV-YB	PRE	877	400	45.6	42.3	49.0
		POST	877	643	73.3	70.3	76.2
	QIV2	PRE	259	28	10.8	7.3	15.2
		POST	259	228	88.0	83.4	91.7
B/Florida/4/2006 (Yamagata)	QIV1	PRE	876	578	66.0	62.7	69.1
		POST	878	869	99.0	98.1	99.5
	TIV-VB	PRE	870	583	67.0	63.8	70.1
		POST	871	805	92.4	90.5	94.1
	TIV-YB	PRE	877	622	70.9	67.8	73.9
		POST	878	873	99.4	98.7	99.8
	QIV2	PRE	259	22	8.5	5.4	12.6
		POST	259	250	96.5	93.5	98.4

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST= Day 28 post last vaccination

7.2.2.2.4. Analysis of Seroconversion factors (ATP-I)

The seroconversion factors (SCFs), i.e., the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination, are shown in Table 35 for all subjects and in Supplement 23 by age groups.

The SCFs ranged from 2.6-fold to 14.4-fold for the vaccine strains in the analysis for all subjects (3 to 17 years old).

The QIV2 group showed robust SCF responses to the FLU Q-QIV vaccine in 6 to 35 month old subjects overall, ranging from 10.9 (A/Victoria/210/2009 [H3N2] strain) to 24.9 (B/Florida/4/2006 Yamagata lineage strain) (Table 35).

Table 35 Seroconversion factor (SCF) for HI antibody titers at 28 days following last vaccination - all subjects (ATP-I)

			SCF		
				95% CI	
Strain	Group	N	Value	LL	UL
A/California/7/2009 (H1N1) (1/DIL)	QIV1	876	12.31	11.34	13.35
	TIV-VB	870	13.31	12.28	14.43
	TIV-YB	877	14.42	13.27	15.66
	QIV2	259	11.95	10.52	13.59
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	876	7.94	7.30	8.64
	TIV-VB	870	7.37	6.78	8.02
	TIV-YB	876	7.78	7.16	8.46
	QIV2	259	10.94	9.64	12.42
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	876	10.12	9.23	11.09
	TIV-VB	870	9.51	8.64	10.45
	TIV-YB	876	2.63	2.47	2.81
	QIV2	259	14.61	12.84	16.63
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	876	8.86	8.12	9.66
	TIV-VB	870	3.37	3.14	3.62
	TIV-YB	877	8.78	8.05	9.58
	QIV2	259	24.92	21.98	28.26

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

7.2.2.2.5. Immunogenicity results by age (ATP-I)

Immunogenicity results by age strata (3-8 years/9-17 years) are presented in Supplement 20 through Supplement 23.

7.2.2.2.6. Immunogenicity results by previous influenza vaccination status (primed or unprimed) (ATP-I)

Immunogenicity results by previous influenza vaccination are presented in Supplement 24 through Supplement 27.

7.2.2.2.7. Reverse cumulative curves for vaccine strain antibody titers (ATP-I)

Reverse cumulative curves (RCCs) for all the vaccine strains also indicated that the immune response was very similar between the FLU Q-QIV and *Fluarix* (VB and YB) treatment groups. The RCCs are shown in Supplement 36 through Supplement 39 for all subjects.

7.3. Total vaccinated cohort (TVC) analysis

Since the percentage of vaccinated subjects excluded from the ATP-I cohort was more than 5%, a second analysis of the primary endpoints based on the TVC was performed to complement the ATP-I analysis. The adjusted GMT ratios and differences in SCRs (with 95% CIs) of the FLU Q-QIV versus *Fluarix* (VB or YB) non-inferiority comparison resulting from the TVC analysis are shown in Supplement 8 through Supplement 15. The adjusted GMT ratios and differences in SCRs (with 95% CIs) of the FLU Q-QIV versus *Fluarix* (VB or YB) superiority contrast (with respect to the non-shared B strain) are shown in Supplement 16 through Supplement 19.

Results from analyses of the secondary endpoints based on the TVC are provided in Supplement 40 through Supplement 43 for all subjects, and by age groups in Supplement 43 through Supplement 47.

The results of all the TVC analyses were consistent with those obtained from the analyses of immunogenicity in the ATP cohort, indicating that no bias was introduced in the selection of subjects complying with the per protocol (ATP-I) analysis.

7.4. Immunogenicity conclusions

- The study met its primary objective of demonstrating immunogenic non-inferiority of the quadrivalent FLU Q-QIV vaccine compared to the trivalent *Fluarix* vaccines, TIV-VB (*Fluarix* containing Victoria B strain) or TIV-YB (*Fluarix* containing Yamagata B strain) after completion of the vaccination series in children 3 to 17 years of age. Both pre-defined statistical acceptance criteria (based on FDA/CBER's guidance) for concluding immunogenic non-inferiority of all four strains in the FLU Q-QIV vaccine were met:

    i. the upper limit of the two-sided 95% confidence interval (CI) of the adjusted GMT ratio (*Fluarix*/FLU Q-QIV) was ≤ 1.5 for each strain (A/H3N2, A/H1N1, VB and YB) contained in the FLU Q-QIV vaccine *and*

    ii. the upper limit of the two-sided 95% CI for the difference in SCR (*Fluarix* minus FLU Q-QIV) was ≤ 10% for each strain (A/H3N2, A/H1N1, VB and YB) contained in the FLU Q-QIV vaccine.

- The study met the confirmatory secondary objective of demonstrating immunogenic superiority of the quadrivalent FLU Q-QIV vaccine over the trivalent *Fluarix* vaccines, TIV-VB (with respect to the *Yamagata* lineage B strain) and TIV-YB (with respect to the *Victoria* lineage B strain) after completion of the vaccination series in children 3 to 17 years of age. Both pre-defined statistical acceptance criteria for inferring immunogenic superiority of QIV vs TIVs for the unique B strain in the QIV vs TIVs were met:

    i. the lower limit of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) was > 1.5 with respect to the B strain present in QIV but absent from the *Fluarix*-TIV (VB or YB) in the specific QIV to TIV comparison (i.e., Q-QIV vs TIV-VB or TIV-YB) *and*

ii. the lower limit of the two-sided 95% CI for the difference in SCR (FLU Q-QIV minus *Fluarix*) was > 10% with respect to the B strain present in QIV but absent from the *Fluarix*-TIV (VB or YB) in the specific QIV to TIV comparison (i.e., Q-QIV vs TIV-VB or TIV-YB).

- The study also achieved its confirmatory secondary objective of demonstrating that, in children 3 to 17 years of age, the immunogenic response to the alternate, Yamagata-lineage, B strain in FLU Q-QIV fulfilled CBER's immunogenicity criteria (lower limit of 95% CI for SCR ≥40% and post-vaccination seroprotection rate [SPR] ≥70%) predictive of clinical benefit.

- The descriptive immunogenicity data (GMT, SCR, SPR, and SCF) indicated that, in children 6 to 35 months of age, each of the four strains in the FLU Q-QIV vaccine met CBER's SCR and SPR criteria (lower limit of 95% CI for SCR ≥40% and post-vaccination seroprotection rate [SPR] ≥70%) indicative of clinical benefit, with the exception of the SPR for A/Victoria/210/2009 (H3N2) strain(LL 95% CI for SPR=68.8%).

8. SAFETY RESULTS

Descriptive summary of safety data is provided in this section. This data, together with the safety data from other studies, will contribute to the safety evaluation of the product (FLU Q-QIV).

8.1. Data sets analyzed

The analysis of safety was performed on the Total vaccinated cohort (TVC). Since the percent of vaccinated subjects excluded from the ATP cohort for analysis of safety (ATP-S) was less than 5% of the TVC, no secondary (complementary) analysis was performed on the ATP-S. See Section 5.10.4 for the definition of the cohorts identified for analyses and Section 6.2 for eligibility for analyses.

8.2. Total vaccinated cohort analysis

The number and percentage of subjects who received study vaccine doses and the compliance in returning symptom sheets are presented in Table 36 and Table 37.

Table 36 Number and percentage of subjects who received study vaccine doses (TVC)

	QIV1 N = 932		TIV-VB N = 929		TIV-YB N = 932		QIV2 N = 301		Total N = 3094	
Total number of doses received	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
1	601	64.5	599	64.5	604	64.8	68	22.6	1872	60.5
2	331	35.5	330	35.5	328	35.2	233	77.4	1222	39.5
Any	932	100	929	100	932	100	301	100	3094	100

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
N = number of subjects in each group or in total included in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose

Table 37 Compliance in returning symptom sheets (TVC)

Dose	Group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
1	QIV1	932	8	912	97.9	913	98.0
	TIV-VB	929	5	911	98.1	911	98.1
	TIV-YB	932	12	914	98.1	915	98.2
	QIV2	301	3	292	97.0	294	97.7
2	QIV1	331	4	323	97.6	324	97.9
	TIV-VB	330	3	321	97.3	322	97.6
	TIV-YB	328	2	317	96.6	318	97.0
	QIV2	233	1	223	95.7	224	96.1
Total	QIV1	1263	12	1235	97.8	1237	97.9
	TIV-VB	1259	8	1232	97.9	1233	97.9
	TIV-YB	1260	14	1231	97.7	1233	97.9
	QIV2	534	4	515	96.4	518	97.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
SS = Symptom sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom sheet return / number of administered doses) X 100

8.2.1. Overall incidence of adverse events

The overall incidence of solicited and unsolicited AEs during the 7-day post-vaccination period is presented in Table 38 (any grade) and Table 39 (grade 3). The overall incidence and nature of causally related solicited and unsolicited AEs during the 7-Day post-vaccination period is presented in Supplement 60 (any grade) and Supplement 61 (grade 3).

For subjects 3 to 17 years old (overall/subject):

Any solicited and unsolicited AEs were reported for 77.3%, 71.6%, and 69.0% of subjects in the Q-QIV, TIV-VB, and TIV-YB groups, respectively, with any grade 3 symptoms reported for 7.6%, 7.4%, and 6.4% (Table 38 and Table 39).

For subjects 6 to 35 months old receiving FLU Q-QIV only (QIV2 group) (overall/subject):

Any solicited and unsolicited AEs were reported for 74.8% of subjects with grade 3 symptoms reported for 10.3% (Table 38 and Table 39).

Table 38 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (TVC)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	QIV1	932	690	74.0	71.1	76.8	932	453	48.6	45.4	51.9	932	601	64.5	61.3	67.6
	TIV-VB	929	625	67.3	64.2	70.3	929	437	47.0	43.8	50.3	929	506	54.5	51.2	57.7
	TIV-YB	932	619	66.4	63.3	69.4	932	444	47.6	44.4	50.9	932	515	55.3	52.0	58.5
	QIV2	301	206	68.4	62.9	73.7	301	168	55.8	50.0	61.5	301	137	45.5	39.8	51.3
Dose 2	QIV1	331	197	59.5	54.0	64.8	331	112	33.8	28.8	39.2	331	171	51.7	46.1	57.2
	TIV-VB	330	190	57.6	52.0	63.0	330	108	32.7	27.7	38.1	330	155	47.0	41.5	52.5
	TIV-YB	328	171	52.1	46.6	57.7	328	92	28.0	23.3	33.2	328	145	44.2	38.8	49.8
	QIV2	233	131	56.2	49.6	62.7	233	104	44.6	38.1	51.3	233	85	36.5	30.3	43.0
Overall/dose	QIV1	1263	887	70.2	67.6	72.7	1263	565	44.7	42.0	47.5	1263	772	61.1	58.4	63.8
	TIV-VB	1259	815	64.7	62.0	67.4	1259	545	43.3	40.5	46.1	1259	661	52.5	49.7	55.3
	TIV-YB	1260	790	62.7	60.0	65.4	1260	536	42.5	39.8	45.3	1260	660	52.4	49.6	55.2
	QIV2	534	337	63.1	58.9	67.2	534	272	50.9	46.6	55.3	534	222	41.6	37.4	45.9
Overall/subject	QIV1	932	720	77.3	74.4	79.9	932	484	51.9	48.7	55.2	932	642	68.9	65.8	71.8
	TIV-VB	929	665	71.6	68.6	74.5	929	479	51.6	48.3	54.8	929	550	59.2	56.0	62.4
	TIV-YB	932	643	69.0	65.9	72.0	932	470	50.4	47.2	53.7	932	546	58.6	55.3	61.8
	QIV2	301	225	74.8	69.4	79.6	301	193	64.1	58.4	69.5	301	156	51.8	46.0	57.6

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 39 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	QIV1	932	56	6.0	4.6	7.7	932	30	3.2	2.2	4.6	932	31	3.3	2.3	4.7
	TIV-VB	929	53	5.7	4.3	7.4	929	41	4.4	3.2	5.9	929	16	1.7	1.0	2.8
	TIV-YB	932	50	5.4	4.0	7.0	932	35	3.8	2.6	5.2	932	22	2.4	1.5	3.6
	QIV2	301	19	6.3	3.8	9.7	301	16	5.3	3.1	8.5	301	3	1.0	0.2	2.9
Dose 2	QIV1	331	16	4.8	2.8	7.7	331	11	3.3	1.7	5.9	331	6	1.8	0.7	3.9
	TIV-VB	330	18	5.5	3.3	8.5	330	14	4.2	2.3	7.0	330	5	1.5	0.5	3.5
	TIV-YB	328	13	4.0	2.1	6.7	328	8	2.4	1.1	4.7	328	6	1.8	0.7	3.9
	QIV2	233	18	7.7	4.6	11.9	233	14	6.0	3.3	9.9	233	6	2.6	1.0	5.5
Overall/dose	QIV1	1263	72	5.7	4.5	7.1	1263	41	3.2	2.3	4.4	1263	37	2.9	2.1	4.0
	TIV-VB	1259	71	5.6	4.4	7.1	1259	55	4.4	3.3	5.6	1259	21	1.7	1.0	2.5
	TIV-YB	1260	63	5.0	3.9	6.4	1260	43	3.4	2.5	4.6	1260	28	2.2	1.5	3.2
	QIV2	534	37	6.9	4.9	9.4	534	30	5.6	3.8	7.9	534	9	1.7	0.8	3.2
Overall/subject	QIV1	932	71	7.6	6.0	9.5	932	41	4.4	3.2	5.9	932	37	4.0	2.8	5.4
	TIV-VB	929	69	7.4	5.8	9.3	929	53	5.7	4.3	7.4	929	21	2.3	1.4	3.4
	TIV-YB	932	60	6.4	4.9	8.2	932	43	4.6	3.4	6.2	932	26	2.8	1.8	4.1
	QIV2	301	31	10.3	7.1	14.3	301	26	8.6	5.7	12.4	301	8	2.7	1.2	5.2

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

8.2.2. Solicited local adverse events

The incidence of solicited local AEs (all grade/grade 3) during the 7-day post-vaccination period is presented in Table 40.

For subjects 3 to 17 years old (overall/subject):

Injection site pain was the most frequently reported local AE across the three treatment groups (reported for 69.8%, 59.0%, and 59.2% of subjects in the QIV1, TIV-VB, and TIV-YB groups, respectively). Redness was reported for 6.2% to 3.9% of subjects and swelling for 7.0% to 4.3%. Grade 3 injection site pain was reported for 3.8%, 2.3% and 2.8% of subjects in the QIV1, TIV-VB, and TIV-YB groups, respectively, grade 3 redness for 0.1%, 0.0% and 0.0% of subjects and grade 3 swelling for 0.1%, 0.0% and 0.0% of subjects (Table 40).

For subjects 6 to 35 months old receiving Q-QIV (QIV2 group) (overall/subject):

Injection site pain and redness were the most frequently reported local AEs (reported for 50.3% and 8.2% of subjects, respectively). Grade 3 injection site pain and grade 3

redness were reported for 2.0% and 0.7% of subjects, respectively. Grade 3 swelling was reported for 0.3% of subjects (Table 40).

All solicited local symptoms were considered to be causally related to vaccination by protocol definition.

Further detailed information on the incidence of solicited local AEs (all grade/grade 3) during the 7-day post-vaccination period (analyzed by age strata) is presented in Supplement 62.

The duration (number of days) of the local solicited symptoms is presented in Supplement 63. The mean duration of local solicited symptoms (overall/dose) during the 7-day post-vaccination period in the QIV1, TIV-VB, and TIV-YB groups ranged from 1.9 to 2.3 days and in the QIV2 group, the mean duration ranged from 1.9 to 2.7 days.

Table 40 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (TVC)

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Pain	All	913	597	65.4	62.2	68.5	911	497	54.6	51.3	57.8	915	510	55.7	52.5	59.0
	Grade 2*3	913	189	20.7	18.1	23.5	911	118	13.0	10.8	15.3	915	130	14.2	12.0	16.6
	Grade 3	913	29	3.2	2.1	4.5	911	16	1.8	1.0	2.8	915	22	2.4	1.5	3.6
	Med adv	913	0	0.0	0.0	0.4	911	0	0.0	0.0	0.4	915	0	0.0	0.0	0.4
Redness (mm)	All	913	48	5.3	3.9	6.9	911	29	3.2	2.1	4.5	915	32	3.5	2.4	4.9
	[50 - ...	913	24	2.6	1.7	3.9	911	6	0.7	0.2	1.4	915	8	0.9	0.4	1.7
	>100	913	1	0.1	0.0	0.6	911	0	0.0	0.0	0.4	915	0	0.0	0.0	0.4
	Med adv	913	4	0.4	0.1	1.1	911	1	0.1	0.0	0.6	915	0	0.0	0.0	0.4
Swelling (mm)	All	913	57	6.2	4.8	8.0	911	30	3.3	2.2	4.7	915	35	3.8	2.7	5.3
	[50 - ...	913	23	2.5	1.6	3.8	911	3	0.3	0.1	1.0	915	12	1.3	0.7	2.3
	>100	913	1	0.1	0.0	0.6	911	0	0.0	0.0	0.4	915	0	0.0	0.0	0.4
	Med adv	913	2	0.2	0.0	0.8	911	0	0.0	0.0	0.4	915	0	0.0	0.0	0.4
Dose 2																
Pain	All	324	169	52.2	46.6	57.7	322	151	46.9	41.3	52.5	318	141	44.3	38.8	50.0
	Grade 2*3	324	48	14.8	11.1	19.2	322	34	10.6	7.4	14.4	318	33	10.4	7.3	14.3
	Grade 3	324	6	1.9	0.7	4.0	322	5	1.6	0.5	3.6	318	6	1.9	0.7	4.1
	Med adv	324	0	0.0	0.0	1.1	322	0	0.0	0.0	1.1	318	0	0.0	0.0	1.2
Redness (mm)	All	324	13	4.0	2.2	6.8	322	11	3.4	1.7	6.0	318	10	3.1	1.5	5.7
	[50 - ...	324	6	1.9	0.7	4.0	322	5	1.6	0.5	3.6	318	4	1.3	0.3	3.2
	>100	324	0	0.0	0.0	1.1	322	0	0.0	0.0	1.1	318	0	0.0	0.0	1.2
	Med adv	324	0	0.0	0.0	1.1	322	0	0.0	0.0	1.1	318	0	0.0	0.0	1.2
Swelling (mm)	All	324	12	3.7	1.9	6.4	322	15	4.7	2.6	7.6	318	7	2.2	0.9	4.5
	[50 - ...	324	6	1.9	0.7	4.0	322	3	0.9	0.2	2.7	318	2	0.6	0.1	2.3
	>100	324	0	0.0	0.0	1.1	322	0	0.0	0.0	1.1	318	0	0.0	0.0	1.2
	Med adv	324	0	0.0	0.0	1.1	322	0	0.0	0.0	1.1	318	0	0.0	0.0	1.2
Overall/dose																
Pain	All	1237	766	61.9	59.2	64.6	1233	648	52.6	49.7	55.4	1233	651	52.8	50.0	55.6
	Grade 2*3	1237	237	19.2	17.0	21.5	1233	152	12.3	10.5	14.3	1233	163	13.2	11.4	15.2
	Grade 3	1237	35	2.8	2.0	3.9	1233	21	1.7	1.1	2.6	1233	28	2.3	1.5	3.3
	Med adv	1237	0	0.0	0.0	0.3	1233	0	0.0	0.0	0.3	1233	0	0.0	0.0	0.3
Redness (mm)	All	1237	61	4.9	3.8	6.3	1233	40	3.2	2.3	4.4	1233	42	3.4	2.5	4.6
	[50 - ...	1237	30	2.4	1.6	3.4	1233	11	0.9	0.4	1.6	1233	12	1.0	0.5	1.7
	>100	1237	1	0.1	0.0	0.4	1233	0	0.0	0.0	0.3	1233	0	0.0	0.0	0.3
	Med adv	1237	4	0.3	0.1	0.8	1233	1	0.1	0.0	0.5	1233	0	0.0	0.0	0.3
Swelling (mm)	All	1237	69	5.6	4.4	7.0	1233	45	3.6	2.7	4.9	1233	42	3.4	2.5	4.6
	[50 - ...	1237	29	2.3	1.6	3.3	1233	6	0.5	0.2	1.1	1233	14	1.1	0.6	1.9
	>100	1237	1	0.1	0.0	0.4	1233	0	0.0	0.0	0.3	1233	0	0.0	0.0	0.3
	Med adv	1237	2	0.2	0.0	0.6	1233	0	0.0	0.0	0.3	1233	0	0.0	0.0	0.3
Overall/subject																
Pain	All	913	637	69.8	66.7	72.7	912	538	59.0	55.7	62.2	916	542	59.2	55.9	62.4
	Grade 2*3	913	216	23.7	20.9	26.6	912	142	15.6	13.3	18.1	916	149	16.3	13.9	18.8
	Grade 3	913	35	3.8	2.7	5.3	912	21	2.3	1.4	3.5	916	26	2.8	1.9	4.1
	Med adv	913	0	0.0	0.0	0.4	912	0	0.0	0.0	0.4	916	0	0.0	0.0	0.4
Redness (mm)	All	913	57	6.2	4.8	8.0	912	38	4.2	3.0	5.7	916	36	3.9	2.8	5.4
	[50 - ...	913	28	3.1	2.0	4.4	912	10	1.1	0.5	2.0	916	9	1.0	0.5	1.9
	>100	913	1	0.1	0.0	0.6	912	0	0.0	0.0	0.4	916	0	0.0	0.0	0.4
	Med adv	913	4	0.4	0.1	1.1	912	1	0.1	0.0	0.6	916	0	0.0	0.0	0.4
Swelling (mm)	All	913	64	7.0	5.4	8.9	912	40	4.4	3.2	5.9	916	39	4.3	3.0	5.8

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	[50 - ...	913	26	2.8	1.9	4.1	912	6	0.7	0.2	1.4	916	12	1.3	0.7	2.3
	>100	913	1	0.1	0.0	0.6	912	0	0.0	0.0	0.4	916	0	0.0	0.0	0.4
	Med adv	913	2	0.2	0.0	0.8	912	0	0.0	0.0	0.4	916	0	0.0	0.0	0.4

		QIV2					Total				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Pain	All	294	131	44.6	38.8	50.4	3033	1735	57.2	55.4	59.0
	Grade 2*3	294	35	11.9	8.4	16.2	3033	472	15.6	14.3	16.9
	Grade 3	294	2	0.7	0.1	2.4	3033	69	2.3	1.8	2.9
	Med adv	294	0	0.0	0.0	1.2	3033	0	0.0	0.0	0.1
Redness (mm)	All	294	13	4.4	2.4	7.4	3033	122	4.0	3.4	4.8
	[50 - ...	294	5	1.7	0.6	3.9	3033	43	1.4	1.0	1.9
	>100	294	1	0.3	0.0	1.9	3033	2	0.1	0.0	0.2
	Med adv	294	0	0.0	0.0	1.2	3033	5	0.2	0.1	0.4
Swelling (mm)	All	294	10	3.4	1.6	6.2	3033	132	4.4	3.7	5.1
	[50 - ...	294	3	1.0	0.2	3.0	3033	41	1.4	1.0	1.8
	>100	294	1	0.3	0.0	1.9	3033	2	0.1	0.0	0.2
	Med adv	294	0	0.0	0.0	1.2	3033	2	0.1	0.0	0.2
Dose 2											
Pain	All	224	76	33.9	27.8	40.5	1188	537	45.2	42.3	48.1
	Grade 2*3	224	19	8.5	5.2	12.9	1188	134	11.3	9.5	13.2
	Grade 3	224	4	1.8	0.5	4.5	1188	21	1.8	1.1	2.7
	Med adv	224	1	0.4	0.0	2.5	1188	1	0.1	0.0	0.5
Redness (mm)	All	224	14	6.3	3.5	10.3	1188	48	4.0	3.0	5.3
	[50 - ...	224	5	2.2	0.7	5.1	1188	20	1.7	1.0	2.6
	>100	224	2	0.9	0.1	3.2	1188	2	0.2	0.0	0.6
	Med adv	224	0	0.0	0.0	1.6	1188	0	0.0	0.0	0.3
Swelling (mm)	All	224	11	4.9	2.5	8.6	1188	45	3.8	2.8	5.0
	[50 - ...	224	5	2.2	0.7	5.1	1188	16	1.3	0.8	2.2
	>100	224	1	0.4	0.0	2.5	1188	1	0.1	0.0	0.5
	Med adv	224	0	0.0	0.0	1.6	1188	0	0.0	0.0	0.3
Overall/dose											
Pain	All	518	207	40.0	35.7	44.3	4221	2272	53.8	52.3	55.3
	Grade 2*3	518	54	10.4	7.9	13.4	4221	606	14.4	13.3	15.5
	Grade 3	518	6	1.2	0.4	2.5	4221	90	2.1	1.7	2.6
	Med adv	518	1	0.2	0.0	1.1	4221	1	0.0	0.0	0.1
Redness (mm)	All	518	27	5.2	3.5	7.5	4221	170	4.0	3.5	4.7
	[50 - ...	518	10	1.9	0.9	3.5	4221	63	1.5	1.1	1.9
	>100	518	3	0.6	0.1	1.7	4221	4	0.1	0.0	0.2
	Med adv	518	0	0.0	0.0	0.7	4221	5	0.1	0.0	0.3
Swelling (mm)	All	518	21	4.1	2.5	6.1	4221	177	4.2	3.6	4.8
	[50 - ...	518	8	1.5	0.7	3.0	4221	57	1.4	1.0	1.7
	>100	518	2	0.4	0.0	1.4	4221	3	0.1	0.0	0.2
	Med adv	518	0	0.0	0.0	0.7	4221	2	0.0	0.0	0.2
Overall/subject											
Pain	All	294	148	50.3	44.5	56.2	3035	1865	61.4	59.7	63.2
	Grade 2*3	294	43	14.6	10.8	19.2	3035	550	18.1	16.8	19.5
	Grade 3	294	6	2.0	0.8	4.4	3035	88	2.9	2.3	3.6
	Med adv	294	1	0.3	0.0	1.9	3035	1	0.0	0.0	0.2
Redness (mm)	All	294	24	8.2	5.3	11.9	3035	155	5.1	4.4	6.0
	[50 - ...	294	8	2.7	1.2	5.3	3035	55	1.8	1.4	2.4

		QIV2					Total				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
	>100	294	2	0.7	0.1	2.4	3035	3	0.1	0.0	0.3
	Med adv	294	0	0.0	0.0	1.2	3035	5	0.2	0.1	0.4
Swelling (mm)	All	294	18	6.1	3.7	9.5	3035	161	5.3	4.5	6.2
	[50 - ...	294	5	1.7	0.6	3.9	3035	49	1.6	1.2	2.1
	>100	294	1	0.3	0.0	1.9	3035	2	0.1	0.0	0.2
	Med adv	294	0	0.0	0.0	1.2	3035	2	0.1	0.0	0.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
Total: n/%= number/percentage of subjects/doses with at least one local symptom whatever the number of injections.
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

8.2.3. Solicited general adverse events

The general symptoms solicited from study subjects younger than 5 years of age were drowsiness, irritability, loss of appetite, and fever (axillary temperature ≥38°C). The general symptoms solicited from study subjects 5 years of age and older were arthralgia (joint pain), fatigue, gastrointestinal symptoms, headache, muscle aches, shivering, and fever (axillary temperature ≥38°C).

The duration (number of days) of the general solicited symptoms is presented in Supplement 64. The mean duration of general solicited symptoms (overall/dose) during the 7-day post-vaccination period in the QIV1, TIV-VB, and TIV-YB groups ranged from 1.5 to 2.4 days and in the QIV2 group, the mean duration ranged from 1.9 to 2.5 days.

Table 41 shows the incidence of solicited general symptoms reported in subjects younger than 5 years of age during the 7-day post-vaccination period and a similar analysis for subjects 5 years and older is presented in Table 42.

For subjects 3 to <5 years old (overall/subject):

Drowsiness (24.9%, 25.1%, and 27.0% of subjects in the Q-QIV, TIV-VB, and TIV-YB groups) and irritability (31.9%, 23.5%, and 25.4%) were the most frequently reported general AEs across the three treatment groups (Table 41).

Grade 3 solicited general AEs, including fever, were reported with a very low incidence rate, ranging from 0.0% to 3.2% (Table 41).

For subjects ≥ 5 to 17 years old (overall/subject):

Muscle ache (30.5%, 26.8%, and 26.6% of subjects), fatigue (23.8%, 24.4%, and 24.4% of subjects), and headache (23.4%, 23.6%, and 21.6% of subjects) were the most frequently reported general AEs across the three treatment groups (Q-QIV, TIV-VB, and TIV-YB groups, respectively) (Table 42).

Grade 3 solicited general AEs, including fever, were reported with a very low incidence rate, ranging from 0.0% to 1.8% (Table 42).

For subjects 6 to 35 months old receiving Q-QIV (QIV2 group) (overall/subject):

Irritability (48.3%) was the most frequently reported general AE followed by drowsiness (34.9%), loss of appetite (31.8%), and temperature (9.2%) (Table 41).

The most frequently reported grade 3 general AEs were loss of appetite (4.3%), irritability (4.8%), and drowsiness (2.4%) (Table 41).

Table 41 Incidence of solicited general symptoms reported by subjects below 5 years of age during the 7-day (Days 0-6) post-vaccination period following each dose and overall (TVC)

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	N	%	LL	UL
Dose 1																
Drowsiness	All	185	39	21.1	15.4	27.7	187	37	19.8	14.3	26.2	189	44	23.3	17.5	30.0
	Grade 2*3	185	6	3.2	1.2	6.9	187	9	4.8	2.2	8.9	189	12	6.3	3.3	10.8
	Grade 3	185	0	0.0	0.0	2.0	187	3	1.6	0.3	4.6	189	1	0.5	0.0	2.9
	Rel	185	30	16.2	11.2	22.3	187	31	16.6	11.6	22.7	189	35	18.5	13.3	24.8
	Grade 3*Rel	185	0	0.0	0.0	2.0	187	2	1.1	0.1	3.8	189	0	0.0	0.0	1.9
	Med adv	185	0	0.0	0.0	2.0	187	1	0.5	0.0	2.9	189	1	0.5	0.0	2.9
Irritability	All	185	48	25.9	19.8	32.9	187	31	16.6	11.6	22.7	189	41	21.7	16.0	28.3
	Grade 2*3	185	9	4.9	2.2	9.0	187	11	5.9	3.0	10.3	189	12	6.3	3.3	10.8
	Grade 3	185	1	0.5	0.0	3.0	187	0	0.0	0.0	2.0	189	3	1.6	0.3	4.6
	Rel	185	37	20.0	14.5	26.5	187	25	13.4	8.8	19.1	189	38	20.1	14.6	26.5
	Grade 3*Rel	185	1	0.5	0.0	3.0	187	0	0.0	0.0	2.0	189	2	1.1	0.1	3.8
	Med adv	185	0	0.0	0.0	2.0	187	1	0.5	0.0	2.9	189	1	0.5	0.0	2.9
Loss of appetite	All	185	32	17.3	12.1	23.5	187	30	16.0	11.1	22.1	189	25	13.2	8.7	18.9
	Grade 2*3	185	2	1.1	0.1	3.9	187	12	6.4	3.4	10.9	189	10	5.3	2.6	9.5
	Grade 3	185	0	0.0	0.0	2.0	187	3	1.6	0.3	4.6	189	2	1.1	0.1	3.8
	Rel	185	19	10.3	6.3	15.6	187	21	11.2	7.1	16.7	189	19	10.1	6.2	15.3
	Grade 3*Rel	185	0	0.0	0.0	2.0	187	2	1.1	0.1	3.8	189	1	0.5	0.0	2.9
	Med adv	185	0	0.0	0.0	2.0	187	2	1.1	0.1	3.8	189	1	0.5	0.0	2.9
Temperature/(Axillary) (°C)	All	185	9	4.9	2.2	9.0	187	11	5.9	3.0	10.3	189	7	3.7	1.5	7.5
	[38 - ...	185	6	3.2	1.2	6.9	187	11	5.9	3.0	10.3	189	6	3.2	1.2	6.8
	[38.5 - ...	185	3	1.6	0.3	4.7	187	6	3.2	1.2	6.9	189	4	2.1	0.6	5.3
	[39 - ...	185	1	0.5	0.0	3.0	187	2	1.1	0.1	3.8	189	3	1.6	0.3	4.6
	[39.6 - ...	185	1	0.5	0.0	3.0	187	1	0.5	0.0	2.9	189	0	0.0	0.0	1.9
	[40.1 - ...	185	0	0.0	0.0	2.0	187	0	0.0	0.0	2.0	189	0	0.0	0.0	1.9
	Rel	185	5	2.7	0.9	6.2	187	7	3.7	1.5	7.6	189	5	2.6	0.9	6.1
	[39 - ...*Rel	185	1	0.5	0.0	3.0	187	0	0.0	0.0	2.0	189	1	0.5	0.0	2.9
	[40.1 - ...*Rel	185	0	0.0	0.0	2.0	187	0	0.0	0.0	2.0	189	0	0.0	0.0	1.9
	Med adv	185	2	1.1	0.1	3.9	187	2	1.1	0.1	3.8	189	3	1.6	0.3	4.6

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**N**	**%**	**LL**	**UL**
Dose 2																
Drowsiness	All	133	16	12.0	7.0	18.8	134	18	13.4	8.2	20.4	131	17	13.0	7.7	20.0
	Grade 2*3	133	5	3.8	1.2	8.6	134	5	3.7	1.2	8.5	131	2	1.5	0.2	5.4
	Grade 3	133	0	0.0	0.0	2.7	134	0	0.0	0.0	2.7	131	0	0.0	0.0	2.8
	Rel	133	12	9.0	4.7	15.2	134	16	11.9	7.0	18.7	131	13	9.9	5.4	16.4
	Grade 3*Rel	133	0	0.0	0.0	2.7	134	0	0.0	0.0	2.7	131	0	0.0	0.0	2.8
	Med adv	133	0	0.0	0.0	2.7	134	0	0.0	0.0	2.7	131	1	0.8	0.0	4.2
Irritability	All	133	25	18.8	12.5	26.5	134	22	16.4	10.6	23.8	131	16	12.2	7.1	19.1
	Grade 2*3	133	5	3.8	1.2	8.6	134	9	6.7	3.1	12.4	131	6	4.6	1.7	9.7
	Grade 3	133	2	1.5	0.2	5.3	134	0	0.0	0.0	2.7	131	0	0.0	0.0	2.8
	Rel	133	20	15.0	9.4	22.3	134	17	12.7	7.6	19.5	131	14	10.7	6.0	17.3
	Grade 3*Rel	133	2	1.5	0.2	5.3	134	0	0.0	0.0	2.7	131	0	0.0	0.0	2.8
	Med adv	133	0	0.0	0.0	2.7	134	1	0.7	0.0	4.1	131	1	0.8	0.0	4.2
Loss of appetite	All	133	13	9.8	5.3	16.1	134	15	11.2	6.4	17.8	131	14	10.7	6.0	17.3
	Grade 2*3	133	4	3.0	0.8	7.5	134	7	5.2	2.1	10.5	131	3	2.3	0.5	6.5
	Grade 3	133	0	0.0	0.0	2.7	134	3	2.2	0.5	6.4	131	1	0.8	0.0	4.2
	Rel	133	6	4.5	1.7	9.6	134	8	6.0	2.6	11.4	131	8	6.1	2.7	11.7
	Grade 3*Rel	133	0	0.0	0.0	2.7	134	1	0.7	0.0	4.1	131	0	0.0	0.0	2.8
	Med adv	133	0	0.0	0.0	2.7	134	2	1.5	0.2	5.3	131	1	0.8	0.0	4.2
Temperature/(Axillary) (°C)	All	133	6	4.5	1.7	9.6	134	6	4.5	1.7	9.5	131	8	6.1	2.7	11.7
	[38 - ...	133	6	4.5	1.7	9.6	134	6	4.5	1.7	9.5	131	8	6.1	2.7	11.7
	[38.5 - ...	133	4	3.0	0.8	7.5	134	3	2.2	0.5	6.4	131	5	3.8	1.3	8.7
	[39 - ...	133	2	1.5	0.2	5.3	134	3	2.2	0.5	6.4	131	2	1.5	0.2	5.4
	[39.6 - ...	133	0	0.0	0.0	2.7	134	0	0.0	0.0	2.7	131	0	0.0	0.0	2.8
	[40.1 - ...	133	0	0.0	0.0	2.7	134	0	0.0	0.0	2.7	131	0	0.0	0.0	2.8
	Rel	133	1	0.8	0.0	4.1	134	4	3.0	0.8	7.5	131	1	0.8	0.0	4.2
	[39 - ...*Rel	133	0	0.0	0.0	2.7	134	2	1.5	0.2	5.3	131	1	0.8	0.0	4.2
	[40.1 - ...*Rel	133	0	0.0	0.0	2.7	134	0	0.0	0.0	2.7	131	0	0.0	0.0	2.8
	Med adv	133	3	2.3	0.5	6.5	134	1	0.7	0.0	4.1	131	4	3.1	0.8	7.6
Overall/dose																
Drowsiness	All	318	55	17.3	13.3	21.9	321	55	17.1	13.2	21.7	320	61	19.1	14.9	23.8
	Grade 2*3	318	11	3.5	1.7	6.1	321	14	4.4	2.4	7.2	320	14	4.4	2.4	7.2
	Grade 3	318	0	0.0	0.0	1.2	321	3	0.9	0.2	2.7	320	1	0.3	0.0	1.7
	Rel	318	42	13.2	9.7	17.4	321	47	14.6	11.0	19.0	320	48	15.0	11.3	19.4
	Grade 3*Rel	318	0	0.0	0.0	1.2	321	2	0.6	0.1	2.2	320	0	0.0	0.0	1.1
	Med adv	318	0	0.0	0.0	1.2	321	1	0.3	0.0	1.7	320	2	0.6	0.1	2.2
Irritability	All	318	73	23.0	18.4	28.0	321	53	16.5	12.6	21.0	320	57	17.8	13.8	22.5
	Grade 2*3	318	14	4.4	2.4	7.3	321	20	6.2	3.8	9.5	320	18	5.6	3.4	8.7
	Grade 3	318	3	0.9	0.2	2.7	321	0	0.0	0.0	1.1	320	3	0.9	0.2	2.7
	Rel	318	57	17.9	13.9	22.6	321	42	13.1	9.6	17.3	320	52	16.3	12.4	20.8
	Grade 3*Rel	318	3	0.9	0.2	2.7	321	0	0.0	0.0	1.1	320	2	0.6	0.1	2.2
	Med adv	318	0	0.0	0.0	1.2	321	2	0.6	0.1	2.2	320	2	0.6	0.1	2.2
Loss of appetite	All	318	45	14.2	10.5	18.5	321	45	14.0	10.4	18.3	320	39	12.2	8.8	16.3
	Grade 2*3	318	6	1.9	0.7	4.1	321	19	5.9	3.6	9.1	320	13	4.1	2.2	6.8
	Grade 3	318	0	0.0	0.0	1.2	321	6	1.9	0.7	4.0	320	3	0.9	0.2	2.7
	Rel	318	25	7.9	5.2	11.4	321	29	9.0	6.1	12.7	320	27	8.4	5.6	12.0
	Grade 3*Rel	318	0	0.0	0.0	1.2	321	3	0.9	0.2	2.7	320	1	0.3	0.0	1.7
	Med adv	318	0	0.0	0.0	1.2	321	4	1.2	0.3	3.2	320	2	0.6	0.1	2.2
Temperature/(Axillary) (°C)	All	318	15	4.7	2.7	7.7	321	17	5.3	3.1	8.3	320	15	4.7	2.6	7.6
	[38 - ...	318	12	3.8	2.0	6.5	321	17	5.3	3.1	8.3	320	14	4.4	2.4	7.2
	[38.5 - ...	318	7	2.2	0.9	4.5	321	9	2.8	1.3	5.3	320	9	2.8	1.3	5.3

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	[39 - ...	318	3	0.9	0.2	2.7	321	5	1.6	0.5	3.6	320	5	1.6	0.5	3.6
	[39.6 - ...	318	1	0.3	0.0	1.7	321	1	0.3	0.0	1.7	320	0	0.0	0.0	1.1
	[40.1 - ...	318	0	0.0	0.0	1.2	321	0	0.0	0.0	1.1	320	0	0.0	0.0	1.1
	Rel	318	6	1.9	0.7	4.1	321	11	3.4	1.7	6.0	320	6	1.9	0.7	4.0
	[39 - ...*Rel	318	1	0.3	0.0	1.7	321	2	0.6	0.1	2.2	320	2	0.6	0.1	2.2
	[40.1 - ...*Rel	318	0	0.0	0.0	1.2	321	0	0.0	0.0	1.1	320	0	0.0	0.0	1.1
	Med adv	318	5	1.6	0.5	3.6	321	3	0.9	0.2	2.7	320	7	2.2	0.9	4.5
Overall/subject																
Drowsiness	All	185	46	24.9	18.8	31.7	187	47	25.1	19.1	32.0	189	51	27.0	20.8	33.9
	Grade 2*3	185	11	5.9	3.0	10.4	187	13	7.0	3.8	11.6	189	14	7.4	4.1	12.1
	Grade 3	185	0	0.0	0.0	2.0	187	3	1.6	0.3	4.6	189	1	0.5	0.0	2.9
	Rel	185	34	18.4	13.1	24.7	187	40	21.4	15.7	28.0	189	42	22.2	16.5	28.8
	Grade 3*Rel	185	0	0.0	0.0	2.0	187	2	1.1	0.1	3.8	189	0	0.0	0.0	1.9
	Med adv	185	0	0.0	0.0	2.0	187	1	0.5	0.0	2.9	189	2	1.1	0.1	3.8
Irritability	All	185	59	31.9	25.2	39.1	187	44	23.5	17.6	30.3	189	48	25.4	19.4	32.2
	Grade 2*3	185	12	6.5	3.4	11.1	187	17	9.1	5.4	14.2	189	15	7.9	4.5	12.8
	Grade 3	185	3	1.6	0.3	4.7	187	0	0.0	0.0	2.0	189	3	1.6	0.3	4.6
	Rel	185	45	24.3	18.3	31.2	187	36	19.3	13.9	25.6	189	45	23.8	17.9	30.5
	Grade 3*Rel	185	3	1.6	0.3	4.7	187	0	0.0	0.0	2.0	189	2	1.1	0.1	3.8
	Med adv	185	0	0.0	0.0	2.0	187	2	1.1	0.1	3.8	189	2	1.1	0.1	3.8
Loss of appetite	All	185	40	21.6	15.9	28.3	187	41	21.9	16.2	28.5	189	35	18.5	13.3	24.8
	Grade 2*3	185	6	3.2	1.2	6.9	187	18	9.6	5.8	14.8	189	11	5.8	2.9	10.2
	Grade 3	185	0	0.0	0.0	2.0	187	6	3.2	1.2	6.9	189	3	1.6	0.3	4.6
	Rel	185	21	11.4	7.2	16.8	187	28	15.0	10.2	20.9	189	24	12.7	8.3	18.3
	Grade 3*Rel	185	0	0.0	0.0	2.0	187	3	1.6	0.3	4.6	189	1	0.5	0.0	2.9
	Med adv	185	0	0.0	0.0	2.0	187	4	2.1	0.6	5.4	189	2	1.1	0.1	3.8
Temperature/(Axillary) (°C)	All	185	15	8.1	4.6	13.0	187	16	8.6	5.0	13.5	189	15	7.9	4.5	12.8
	[38 - ...	185	12	6.5	3.4	11.1	187	16	8.6	5.0	13.5	189	14	7.4	4.1	12.1
	[38.5 - ...	185	7	3.8	1.5	7.6	187	9	4.8	2.2	8.9	189	9	4.8	2.2	8.8
	[39 - ...	185	3	1.6	0.3	4.7	187	5	2.7	0.9	6.1	189	5	2.6	0.9	6.1
	[39.6 - ...	185	1	0.5	0.0	3.0	187	1	0.5	0.0	2.9	189	0	0.0	0.0	1.9
	[40.1 - ...	185	0	0.0	0.0	2.0	187	0	0.0	0.0	2.0	189	0	0.0	0.0	1.9
	Rel	185	6	3.2	1.2	6.9	187	10	5.3	2.6	9.6	189	6	3.2	1.2	6.8
	[39 - ...*Rel	185	1	0.5	0.0	3.0	187	2	1.1	0.1	3.8	189	2	1.1	0.1	3.8
	[40.1 - ...*Rel	185	0	0.0	0.0	2.0	187	0	0.0	0.0	2.0	189	0	0.0	0.0	1.9
	Med adv	185	5	2.7	0.9	6.2	187	3	1.6	0.3	4.6	189	7	3.7	1.5	7.5

		QIV2					Total				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Drowsiness	All	292	85	29.1	24.0	34.7	853	205	24.0	21.2	27.0
	Grade 2*3	292	22	7.5	4.8	11.2	853	49	5.7	4.3	7.5
	Grade 3	292	6	2.1	0.8	4.4	853	10	1.2	0.6	2.1
	Rel	292	77	26.4	21.4	31.8	853	173	20.3	17.6	23.1
	Grade 3*Rel	292	6	2.1	0.8	4.4	853	8	0.9	0.4	1.8
	Med adv	292	3	1.0	0.2	3.0	853	5	0.6	0.2	1.4
Irritability	All	292	120	41.1	35.4	47.0	853	240	28.1	25.1	31.3
	Grade 2*3	292	43	14.7	10.9	19.3	853	75	8.8	7.0	10.9
	Grade 3	292	8	2.7	1.2	5.3	853	12	1.4	0.7	2.4
	Rel	292	105	36.0	30.5	41.8	853	205	24.0	21.2	27.0
	Grade 3*Rel	292	7	2.4	1.0	4.9	853	10	1.2	0.6	2.1

		QIV2					Total				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Med adv	292	4	1.4	0.4	3.5	853	6	0.7	0.3	1.5
Loss of appetite	All	292	64	21.9	17.3	27.1	853	151	17.7	15.2	20.4
	Grade 2*3	292	15	5.1	2.9	8.3	853	39	4.6	3.3	6.2
	Grade 3	292	3	1.0	0.2	3.0	853	8	0.9	0.4	1.8
	Rel	292	48	16.4	12.4	21.2	853	107	12.5	10.4	15.0
	Grade 3*Rel	292	3	1.0	0.2	3.0	853	6	0.7	0.3	1.5
	Med adv	292	3	1.0	0.2	3.0	853	6	0.7	0.3	1.5
Temperature/(Axillary) (°C)	All	292	16	5.5	3.2	8.7	853	43	5.0	3.7	6.7
	[38 - ...	292	13	4.5	2.4	7.5	853	36	4.2	3.0	5.8
	[38.5 - ...	292	4	1.4	0.4	3.5	853	17	2.0	1.2	3.2
	[39 - ...	292	3	1.0	0.2	3.0	853	9	1.1	0.5	2.0
	[39.6 - ...	292	2	0.7	0.1	2.5	853	4	0.5	0.1	1.2
	[40.1 - ...	292	0	0.0	0.0	1.3	853	0	0.0	0.0	0.4
	Rel	292	11	3.8	1.9	6.6	853	28	3.3	2.2	4.7
	[39 - ...*Rel	292	2	0.7	0.1	2.5	853	4	0.5	0.1	1.2
	[40.1 - ...*Rel	292	0	0.0	0.0	1.3	853	0	0.0	0.0	0.4
	Med adv	292	2	0.7	0.1	2.5	853	9	1.1	0.5	2.0
Dose 2											
Drowsiness	All	223	45	20.2	15.1	26.1	621	96	15.5	12.7	18.5
	Grade 2*3	223	16	7.2	4.2	11.4	621	28	4.5	3.0	6.5
	Grade 3	223	2	0.9	0.1	3.2	621	2	0.3	0.0	1.2
	Rel	223	37	16.6	12.0	22.1	621	78	12.6	10.1	15.4
	Grade 3*Rel	223	2	0.9	0.1	3.2	621	2	0.3	0.0	1.2
	Med adv	223	4	1.8	0.5	4.5	621	5	0.8	0.3	1.9
Irritability	All	223	74	33.2	27.0	39.8	621	137	22.1	18.9	25.5
	Grade 2*3	223	32	14.3	10.0	19.6	621	52	8.4	6.3	10.8
	Grade 3	223	8	3.6	1.6	6.9	621	10	1.6	0.8	2.9
	Rel	223	66	29.6	23.7	36.1	621	117	18.8	15.8	22.1
	Grade 3*Rel	223	4	1.8	0.5	4.5	621	6	1.0	0.4	2.1
	Med adv	223	5	2.2	0.7	5.2	621	7	1.1	0.5	2.3
Loss of appetite	All	223	48	21.5	16.3	27.5	621	90	14.5	11.8	17.5
	Grade 2*3	223	15	6.7	3.8	10.9	621	29	4.7	3.1	6.6
	Grade 3	223	3	1.3	0.3	3.9	621	7	1.1	0.5	2.3
	Rel	223	40	17.9	13.1	23.6	621	62	10.0	7.7	12.6
	Grade 3*Rel	223	3	1.3	0.3	3.9	621	4	0.6	0.2	1.6
	Med adv	223	3	1.3	0.3	3.9	621	6	1.0	0.4	2.1
Temperature/(Axillary) (°C)	All	223	12	5.4	2.8	9.2	621	32	5.2	3.6	7.2
	[38 - ...	223	12	5.4	2.8	9.2	621	32	5.2	3.6	7.2
	[38.5 - ...	223	7	3.1	1.3	6.4	621	19	3.1	1.9	4.7
	[39 - ...	223	3	1.3	0.3	3.9	621	10	1.6	0.8	2.9
	[39.6 - ...	223	1	0.4	0.0	2.5	621	1	0.2	0.0	0.9
	[40.1 - ...	223	1	0.4	0.0	2.5	621	1	0.2	0.0	0.9
	Rel	223	8	3.6	1.6	6.9	621	14	2.3	1.2	3.8
	[39 - ...*Rel	223	1	0.4	0.0	2.5	621	4	0.6	0.2	1.6
	[40.1 - ...*Rel	223	0	0.0	0.0	1.6	621	0	0.0	0.0	0.6
	Med adv	223	4	1.8	0.5	4.5	621	12	1.9	1.0	3.4
Overall/dose											
Drowsiness	All	515	130	25.2	21.5	29.2	1474	301	20.4	18.4	22.6
	Grade 2*3	515	38	7.4	5.3	10.0	1474	77	5.2	4.1	6.5
	Grade 3	515	8	1.6	0.7	3.0	1474	12	0.8	0.4	1.4
	Rel	515	114	22.1	18.6	26.0	1474	251	17.0	15.1	19.0

		QIV2					Total				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3*Rel	515	8	1.6	0.7	3.0	1474	10	0.7	0.3	1.2
	Med adv	515	7	1.4	0.5	2.8	1474	10	0.7	0.3	1.2
Irritability	All	515	194	37.7	33.5	42.0	1474	377	25.6	23.4	27.9
	Grade 2*3	515	75	14.6	11.6	17.9	1474	127	8.6	7.2	10.2
	Grade 3	515	16	3.1	1.8	5.0	1474	22	1.5	0.9	2.3
	Rel	515	171	33.2	29.1	37.5	1474	322	21.8	19.8	24.0
	Grade 3*Rel	515	11	2.1	1.1	3.8	1474	16	1.1	0.6	1.8
	Med adv	515	9	1.7	0.8	3.3	1474	13	0.9	0.5	1.5
Loss of appetite	All	515	112	21.7	18.3	25.6	1474	241	16.4	14.5	18.3
	Grade 2*3	515	30	5.8	4.0	8.2	1474	68	4.6	3.6	5.8
	Grade 3	515	6	1.2	0.4	2.5	1474	15	1.0	0.6	1.7
	Rel	515	88	17.1	13.9	20.6	1474	169	11.5	9.9	13.2
	Grade 3*Rel	515	6	1.2	0.4	2.5	1474	10	0.7	0.3	1.2
	Med adv	515	6	1.2	0.4	2.5	1474	12	0.8	0.4	1.4
Temperature/(Axillary) (°C)	All	515	28	5.4	3.6	7.8	1474	75	5.1	4.0	6.3
	[38 - ...	515	25	4.9	3.2	7.1	1474	68	4.6	3.6	5.8
	[38.5 - ...	515	11	2.1	1.1	3.8	1474	36	2.4	1.7	3.4
	[39 - ...	515	6	1.2	0.4	2.5	1474	19	1.3	0.8	2.0
	[39.6 - ...	515	3	0.6	0.1	1.7	1474	5	0.3	0.1	0.8
	[40.1 - ...	515	1	0.2	0.0	1.1	1474	1	0.1	0.0	0.4
	Rel	515	19	3.7	2.2	5.7	1474	42	2.8	2.1	3.8
	[39 - ...*Rel	515	3	0.6	0.1	1.7	1474	8	0.5	0.2	1.1
	[40.1 - ...*Rel	515	0	0.0	0.0	0.7	1474	0	0.0	0.0	0.2
	Med adv	515	6	1.2	0.4	2.5	1474	21	1.4	0.9	2.2
Overall/subject											
Drowsiness	All	292	102	34.9	29.5	40.7	853	246	28.8	25.8	32.0
	Grade 2*3	292	32	11.0	7.6	15.1	853	70	8.2	6.5	10.3
	Grade 3	292	7	2.4	1.0	4.9	853	11	1.3	0.6	2.3
	Rel	292	93	31.8	26.5	37.5	853	209	24.5	21.6	27.5
	Grade 3*Rel	292	7	2.4	1.0	4.9	853	9	1.1	0.5	2.0
	Med adv	292	7	2.4	1.0	4.9	853	10	1.2	0.6	2.1
Irritability	All	292	141	48.3	42.4	54.2	853	292	34.2	31.0	37.5
	Grade 2*3	292	61	20.9	16.4	26.0	853	105	12.3	10.2	14.7
	Grade 3	292	14	4.8	2.6	7.9	853	20	2.3	1.4	3.6
	Rel	292	130	44.5	38.7	50.4	853	256	30.0	27.0	33.2
	Grade 3*Rel	292	10	3.4	1.7	6.2	853	15	1.8	1.0	2.9
	Med adv	292	8	2.7	1.2	5.3	853	12	1.4	0.7	2.4
Loss of appetite	All	292	93	31.8	26.5	37.5	853	209	24.5	21.6	27.5
	Grade 2*3	292	25	8.6	5.6	12.4	853	60	7.0	5.4	9.0
	Grade 3	292	5	1.7	0.6	4.0	853	14	1.6	0.9	2.7
	Rel	292	73	25.0	20.1	30.4	853	146	17.1	14.6	19.8
	Grade 3*Rel	292	5	1.7	0.6	4.0	853	9	1.1	0.5	2.0
	Med adv	292	6	2.1	0.8	4.4	853	12	1.4	0.7	2.4
Temperature/(Axillary) (°C)	All	292	27	9.2	6.2	13.2	853	73	8.6	6.8	10.6
	[38 - ...	292	24	8.2	5.3	12.0	853	66	7.7	6.0	9.7
	[38.5 - ...	292	11	3.8	1.9	6.6	853	36	4.2	3.0	5.8
	[39 - ...	292	6	2.1	0.8	4.4	853	19	2.2	1.3	3.5
	[39.6 - ...	292	3	1.0	0.2	3.0	853	5	0.6	0.2	1.4
	[40.1 - ...	292	1	0.3	0.0	1.9	853	1	0.1	0.0	0.7
	Rel	292	18	6.2	3.7	9.6	853	40	4.7	3.4	6.3
	[39 - ...*Rel	292	3	1.0	0.2	3.0	853	8	0.9	0.4	1.8

		QIV2					Total				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
	[40.1 - ...*Rel	292	0	0.0	0.0	1.3	853	0	0.0	0.0	0.4
	Med adv	292	6	2.1	0.8	4.4	853	21	2.5	1.5	3.7

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
Total: n/%= number/percentage of subjects/doses with at least one local symptom whatever the number of injections.
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 42 Incidence of solicited general symptoms reported by subjects above 5 years of age during the 7-day (Days 0-6) post-vaccination period following each dose and overall (TVC)

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Fatigue	All	727	161	22.1	19.2	25.3	724	171	23.6	20.6	26.9	725	167	23.0	20.0	26.3
	Grade 2*3	727	37	5.1	3.6	6.9	724	51	7.0	5.3	9.2	725	45	6.2	4.6	8.2
	Grade 3	727	5	0.7	0.2	1.6	724	13	1.8	1.0	3.1	725	7	1.0	0.4	2.0
	Rel	727	133	18.3	15.5	21.3	724	144	19.9	17.0	23.0	725	126	17.4	14.7	20.3
	Grade 3*Rel	727	5	0.7	0.2	1.6	724	7	1.0	0.4	2.0	725	6	0.8	0.3	1.8
	Med adv	727	3	0.4	0.1	1.2	724	5	0.7	0.2	1.6	725	3	0.4	0.1	1.2
Gastrointestinal	All	727	70	9.6	7.6	12.0	724	70	9.7	7.6	12.1	725	65	9.0	7.0	11.3
	Grade 2*3	727	26	3.6	2.3	5.2	724	24	3.3	2.1	4.9	725	16	2.2	1.3	3.6
	Grade 3	727	7	1.0	0.4	2.0	724	7	1.0	0.4	2.0	725	5	0.7	0.2	1.6
	Rel	727	45	6.2	4.6	8.2	724	43	5.9	4.3	7.9	725	32	4.4	3.0	6.2
	Grade 3*Rel	727	4	0.6	0.2	1.4	724	5	0.7	0.2	1.6	725	3	0.4	0.1	1.2
	Med adv	727	2	0.3	0.0	1.0	724	3	0.4	0.1	1.2	725	2	0.3	0.0	1.0
Headache	All	727	160	22.0	19.0	25.2	724	160	22.1	19.1	25.3	725	146	20.1	17.3	23.2
	Grade 2*3	727	38	5.2	3.7	7.1	724	39	5.4	3.9	7.3	725	35	4.8	3.4	6.7
	Grade 3	727	7	1.0	0.4	2.0	724	7	1.0	0.4	2.0	725	9	1.2	0.6	2.3
	Rel	727	122	16.8	14.1	19.7	724	124	17.1	14.5	20.1	725	108	14.9	12.4	17.7
	Grade 3*Rel	727	7	1.0	0.4	2.0	724	3	0.4	0.1	1.2	725	7	1.0	0.4	2.0
	Med adv	727	1	0.1	0.0	0.8	724	6	0.8	0.3	1.8	725	1	0.1	0.0	0.8
Joint pain	All	727	94	12.9	10.6	15.6	724	86	11.9	9.6	14.5	725	76	10.5	8.3	12.9
	Grade 2*3	727	23	3.2	2.0	4.7	724	24	3.3	2.1	4.9	725	16	2.2	1.3	3.6
	Grade 3	727	3	0.4	0.1	1.2	724	4	0.6	0.2	1.4	725	1	0.1	0.0	0.8
	Rel	727	75	10.3	8.2	12.8	724	72	9.9	7.9	12.4	725	63	8.7	6.7	11.0
	Grade 3*Rel	727	3	0.4	0.1	1.2	724	3	0.4	0.1	1.2	725	1	0.1	0.0	0.8
	Med adv	727	2	0.3	0.0	1.0	724	3	0.4	0.1	1.2	725	0	0.0	0.0	0.5
Muscle aches	All	727	207	28.5	25.2	31.9	724	180	24.9	21.8	28.2	725	179	24.7	21.6	28.0
	Grade 2*3	727	47	6.5	4.8	8.5	724	38	5.2	3.7	7.1	725	39	5.4	3.9	7.3
	Grade 3	727	5	0.7	0.2	1.6	724	4	0.6	0.2	1.4	725	7	1.0	0.4	2.0
	Rel	727	187	25.7	22.6	29.1	724	164	22.7	19.7	25.9	725	157	21.7	18.7	24.8
	Grade 3*Rel	727	4	0.6	0.2	1.4	724	3	0.4	0.1	1.2	725	6	0.8	0.3	1.8
	Med adv	727	1	0.1	0.0	0.8	724	5	0.7	0.2	1.6	725	1	0.1	0.0	0.8

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Shivering	All	727	51	7.0	5.3	9.1	724	50	6.9	5.2	9.0	725	50	6.9	5.2	9.0
	Grade 2*3	727	6	0.8	0.3	1.8	724	22	3.0	1.9	4.6	725	18	2.5	1.5	3.9
	Grade 3	727	3	0.4	0.1	1.2	724	9	1.2	0.6	2.3	725	4	0.6	0.2	1.4
	Rel	727	43	5.9	4.3	7.9	724	35	4.8	3.4	6.7	725	40	5.5	4.0	7.4
	Grade 3*Rel	727	2	0.3	0.0	1.0	724	7	1.0	0.4	2.0	725	4	0.6	0.2	1.4
	Med adv	727	2	0.3	0.0	1.0	724	6	0.8	0.3	1.8	725	1	0.1	0.0	0.8
Temperature/(Axillary) (°C)	All	727	16	2.2	1.3	3.5	724	32	4.4	3.0	6.2	725	19	2.6	1.6	4.1
	[38 - ...	727	14	1.9	1.1	3.2	724	26	3.6	2.4	5.2	725	18	2.5	1.5	3.9
	[38.5 - ...	727	6	0.8	0.3	1.8	724	10	1.4	0.7	2.5	725	7	1.0	0.4	2.0
	[39 - ...	727	4	0.6	0.2	1.4	724	8	1.1	0.5	2.2	725	2	0.3	0.0	1.0
	[39.6 - ...	727	2	0.3	0.0	1.0	724	4	0.6	0.2	1.4	725	0	0.0	0.0	0.5
	[40.1 - ...	727	1	0.1	0.0	0.8	724	2	0.3	0.0	1.0	725	0	0.0	0.0	0.5
	Rel	727	10	1.4	0.7	2.5	724	18	2.5	1.5	3.9	725	13	1.8	1.0	3.0
	[39 - ...*Rel	727	3	0.4	0.1	1.2	724	7	1.0	0.4	2.0	725	1	0.1	0.0	0.8
	[40.1 - ...*Rel	727	1	0.1	0.0	0.8	724	2	0.3	0.0	1.0	725	0	0.0	0.0	0.5
	Med adv	727	3	0.4	0.1	1.2	724	5	0.7	0.2	1.6	725	3	0.4	0.1	1.2
Dose 2																
Fatigue	All	190	27	14.2	9.6	20.0	187	19	10.2	6.2	15.4	186	19	10.2	6.3	15.5
	Grade 2*3	190	5	2.6	0.9	6.0	187	3	1.6	0.3	4.6	186	5	2.7	0.9	6.2
	Grade 3	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	1	0.5	0.0	3.0
	Rel	190	25	13.2	8.7	18.8	187	17	9.1	5.4	14.2	186	17	9.1	5.4	14.2
	Grade 3*Rel	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	1	0.5	0.0	3.0
	Med adv	190	0	0.0	0.0	1.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
Gastrointestinal	All	190	17	8.9	5.3	13.9	187	16	8.6	5.0	13.5	186	9	4.8	2.2	9.0
	Grade 2*3	190	5	2.6	0.9	6.0	187	5	2.7	0.9	6.1	186	3	1.6	0.3	4.6
	Grade 3	190	2	1.1	0.1	3.8	187	1	0.5	0.0	2.9	186	1	0.5	0.0	3.0
	Rel	190	14	7.4	4.1	12.1	187	9	4.8	2.2	8.9	186	6	3.2	1.2	6.9
	Grade 3*Rel	190	2	1.1	0.1	3.8	187	0	0.0	0.0	2.0	186	1	0.5	0.0	3.0
	Med adv	190	0	0.0	0.0	1.9	187	1	0.5	0.0	2.9	186	1	0.5	0.0	3.0
Headache	All	190	20	10.5	6.5	15.8	187	19	10.2	6.2	15.4	186	17	9.1	5.4	14.2
	Grade 2*3	190	6	3.2	1.2	6.7	187	6	3.2	1.2	6.9	186	2	1.1	0.1	3.8
	Grade 3	190	1	0.5	0.0	2.9	187	2	1.1	0.1	3.8	186	1	0.5	0.0	3.0
	Rel	190	19	10.0	6.1	15.2	187	16	8.6	5.0	13.5	186	14	7.5	4.2	12.3
	Grade 3*Rel	190	1	0.5	0.0	2.9	187	1	0.5	0.0	2.9	186	0	0.0	0.0	2.0
	Med adv	190	0	0.0	0.0	1.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
Joint pain	All	190	21	11.1	7.0	16.4	187	13	7.0	3.8	11.6	186	10	5.4	2.6	9.7
	Grade 2*3	190	5	2.6	0.9	6.0	187	2	1.1	0.1	3.8	186	1	0.5	0.0	3.0
	Grade 3	190	1	0.5	0.0	2.9	187	1	0.5	0.0	2.9	186	0	0.0	0.0	2.0
	Rel	190	19	10.0	6.1	15.2	187	12	6.4	3.4	10.9	186	8	4.3	1.9	8.3
	Grade 3*Rel	190	1	0.5	0.0	2.9	187	1	0.5	0.0	2.9	186	0	0.0	0.0	2.0
	Med adv	190	0	0.0	0.0	1.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
Muscle aches	All	190	44	23.2	17.4	29.8	187	27	14.4	9.7	20.3	186	30	16.1	11.2	22.2
	Grade 2*3	190	9	4.7	2.2	8.8	187	4	2.1	0.6	5.4	186	7	3.8	1.5	7.6
	Grade 3	190	1	0.5	0.0	2.9	187	1	0.5	0.0	2.9	186	2	1.1	0.1	3.8
	Rel	190	37	19.5	14.1	25.8	187	25	13.4	8.8	19.1	186	27	14.5	9.8	20.4
	Grade 3*Rel	190	1	0.5	0.0	2.9	187	1	0.5	0.0	2.9	186	2	1.1	0.1	3.8
	Med adv	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
Shivering	All	190	8	4.2	1.8	8.1	187	1	0.5	0.0	2.9	186	4	2.2	0.6	5.4
	Grade 2*3	190	3	1.6	0.3	4.5	187	1	0.5	0.0	2.9	186	3	1.6	0.3	4.6
	Grade 3	190	1	0.5	0.0	2.9	187	1	0.5	0.0	2.9	186	0	0.0	0.0	2.0
	Rel	190	6	3.2	1.2	6.7	187	0	0.0	0.0	2.0	186	2	1.1	0.1	3.8
	Grade 3*Rel	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	Med adv	190	0	0.0	0.0	1.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Temperature/(Axillary) (°C)	All	190	11	5.8	2.9	10.1	187	1	0.5	0.0	2.9	186	1	0.5	0.0	3.0
	[38 - ...	190	11	5.8	2.9	10.1	187	1	0.5	0.0	2.9	186	1	0.5	0.0	3.0
	[38.5 - ...	190	6	3.2	1.2	6.7	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	[39 - ...	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	[39.6 - ...	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	[40.1 - ...	190	0	0.0	0.0	1.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	Rel	190	7	3.7	1.5	7.4	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	[39 - ...*Rel	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	[40.1 - ...*Rel	190	0	0.0	0.0	1.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
	Med adv	190	1	0.5	0.0	2.9	187	0	0.0	0.0	2.0	186	0	0.0	0.0	2.0
Overall/dose																
Fatigue	All	917	188	20.5	17.9	23.3	911	190	20.9	18.3	23.6	911	186	20.4	17.8	23.2
	Grade 2*3	917	42	4.6	3.3	6.1	911	54	5.9	4.5	7.7	911	50	5.5	4.1	7.2
	Grade 3	917	6	0.7	0.2	1.4	911	13	1.4	0.8	2.4	911	8	0.9	0.4	1.7
	Rel	917	158	17.2	14.8	19.8	911	161	17.7	15.2	20.3	911	143	15.7	13.4	18.2
	Grade 3*Rel	917	6	0.7	0.2	1.4	911	7	0.8	0.3	1.6	911	7	0.8	0.3	1.6
	Med adv	917	3	0.3	0.1	1.0	911	5	0.5	0.2	1.3	911	3	0.3	0.1	1.0
Gastrointestinal	All	917	87	9.5	7.7	11.6	911	86	9.4	7.6	11.5	911	74	8.1	6.4	10.1
	Grade 2*3	917	31	3.4	2.3	4.8	911	29	3.2	2.1	4.5	911	19	2.1	1.3	3.2
	Grade 3	917	9	1.0	0.4	1.9	911	8	0.9	0.4	1.7	911	6	0.7	0.2	1.4
	Rel	917	59	6.4	4.9	8.2	911	52	5.7	4.3	7.4	911	38	4.2	3.0	5.7
	Grade 3*Rel	917	6	0.7	0.2	1.4	911	5	0.5	0.2	1.3	911	4	0.4	0.1	1.1
	Med adv	917	2	0.2	0.0	0.8	911	4	0.4	0.1	1.1	911	3	0.3	0.1	1.0
Headache	All	917	180	19.6	17.1	22.4	911	179	19.6	17.1	22.4	911	163	17.9	15.5	20.5
	Grade 2*3	917	44	4.8	3.5	6.4	911	45	4.9	3.6	6.6	911	37	4.1	2.9	5.6
	Grade 3	917	8	0.9	0.4	1.7	911	9	1.0	0.5	1.9	911	10	1.1	0.5	2.0
	Rel	917	141	15.4	13.1	17.9	911	140	15.4	13.1	17.9	911	122	13.4	11.2	15.8
	Grade 3*Rel	917	8	0.9	0.4	1.7	911	4	0.4	0.1	1.1	911	7	0.8	0.3	1.6
	Med adv	917	1	0.1	0.0	0.6	911	6	0.7	0.2	1.4	911	1	0.1	0.0	0.6
Joint pain	All	917	115	12.5	10.5	14.9	911	99	10.9	8.9	13.1	911	86	9.4	7.6	11.5
	Grade 2*3	917	28	3.1	2.0	4.4	911	26	2.9	1.9	4.2	911	17	1.9	1.1	3.0
	Grade 3	917	4	0.4	0.1	1.1	911	5	0.5	0.2	1.3	911	1	0.1	0.0	0.6
	Rel	917	94	10.3	8.4	12.4	911	84	9.2	7.4	11.3	911	71	7.8	6.1	9.7
	Grade 3*Rel	917	4	0.4	0.1	1.1	911	4	0.4	0.1	1.1	911	1	0.1	0.0	0.6
	Med adv	917	2	0.2	0.0	0.8	911	3	0.3	0.1	1.0	911	0	0.0	0.0	0.4
Muscle aches	All	917	251	27.4	24.5	30.4	911	207	22.7	20.0	25.6	911	209	22.9	20.2	25.8
	Grade 2*3	917	56	6.1	4.6	7.9	911	42	4.6	3.3	6.2	911	46	5.0	3.7	6.7
	Grade 3	917	6	0.7	0.2	1.4	911	5	0.5	0.2	1.3	911	9	1.0	0.5	1.9
	Rel	917	224	24.4	21.7	27.3	911	189	20.7	18.2	23.5	911	184	20.2	17.6	23.0
	Grade 3*Rel	917	5	0.5	0.2	1.3	911	4	0.4	0.1	1.1	911	8	0.9	0.4	1.7
	Med adv	917	2	0.2	0.0	0.8	911	5	0.5	0.2	1.3	911	1	0.1	0.0	0.6
Shivering	All	917	59	6.4	4.9	8.2	911	51	5.6	4.2	7.3	911	54	5.9	4.5	7.7
	Grade 2*3	917	9	1.0	0.4	1.9	911	23	2.5	1.6	3.8	911	21	2.3	1.4	3.5
	Grade 3	917	4	0.4	0.1	1.1	911	10	1.1	0.5	2.0	911	4	0.4	0.1	1.1
	Rel	917	49	5.3	4.0	7.0	911	35	3.8	2.7	5.3	911	42	4.6	3.3	6.2
	Grade 3*Rel	917	3	0.3	0.1	1.0	911	7	0.8	0.3	1.6	911	4	0.4	0.1	1.1
	Med adv	917	2	0.2	0.0	0.8	911	6	0.7	0.2	1.4	911	1	0.1	0.0	0.6
Temperature/(Axillary) (°C)	All	917	27	2.9	1.9	4.3	911	33	3.6	2.5	5.0	911	20	2.2	1.3	3.4
	[38 - ...	917	25	2.7	1.8	4.0	911	27	3.0	2.0	4.3	911	19	2.1	1.3	3.2
	[38.5 - ...	917	12	1.3	0.7	2.3	911	10	1.1	0.5	2.0	911	7	0.8	0.3	1.6
	[39 - ...	917	5	0.5	0.2	1.3	911	8	0.9	0.4	1.7	911	2	0.2	0.0	0.8
	[39.6 - ...	917	3	0.3	0.1	1.0	911	4	0.4	0.1	1.1	911	0	0.0	0.0	0.4
	[40.1 - ...	917	1	0.1	0.0	0.6	911	2	0.2	0.0	0.8	911	0	0.0	0.0	0.4

		QIV1					TIV-VB					TIV-YB				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Rel	917	17	1.9	1.1	3.0	911	18	2.0	1.2	3.1	911	13	1.4	0.8	2.4
	[39 - ...*Rel	917	4	0.4	0.1	1.1	911	7	0.8	0.3	1.6	911	1	0.1	0.0	0.6
	[40.1 - ...*Rel	917	1	0.1	0.0	0.6	911	2	0.2	0.0	0.8	911	0	0.0	0.0	0.4
	Med adv	917	4	0.4	0.1	1.1	911	5	0.5	0.2	1.3	911	3	0.3	0.1	1.0
Overall/subject																
Fatigue	All	727	173	23.8	20.7	27.1	725	177	24.4	21.3	27.7	726	177	24.4	21.3	27.7
	Grade 2*3	727	41	5.6	4.1	7.6	725	53	7.3	5.5	9.5	726	49	6.7	5.0	8.8
	Grade 3	727	6	0.8	0.3	1.8	725	13	1.8	1.0	3.0	726	8	1.1	0.5	2.2
	Rel	727	143	19.7	16.8	22.7	725	149	20.6	17.7	23.7	726	134	18.5	15.7	21.5
	Grade 3*Rel	727	6	0.8	0.3	1.8	725	7	1.0	0.4	2.0	726	7	1.0	0.4	2.0
	Med adv	727	3	0.4	0.1	1.2	725	5	0.7	0.2	1.6	726	3	0.4	0.1	1.2
Gastrointestinal	All	727	80	11.0	8.8	13.5	725	82	11.3	9.1	13.8	726	72	9.9	7.8	12.3
	Grade 2*3	727	29	4.0	2.7	5.7	725	29	4.0	2.7	5.7	726	19	2.6	1.6	4.1
	Grade 3	727	9	1.2	0.6	2.3	725	8	1.1	0.5	2.2	726	6	0.8	0.3	1.8
	Rel	727	55	7.6	5.7	9.7	725	51	7.0	5.3	9.1	726	37	5.1	3.6	7.0
	Grade 3*Rel	727	6	0.8	0.3	1.8	725	5	0.7	0.2	1.6	726	4	0.6	0.2	1.4
	Med adv	727	2	0.3	0.0	1.0	725	4	0.6	0.2	1.4	726	3	0.4	0.1	1.2
Headache	All	727	170	23.4	20.4	26.6	725	171	23.6	20.5	26.8	726	157	21.6	18.7	24.8
	Grade 2*3	727	44	6.1	4.4	8.0	725	44	6.1	4.4	8.1	726	37	5.1	3.6	7.0
	Grade 3	727	8	1.1	0.5	2.2	725	9	1.2	0.6	2.3	726	10	1.4	0.7	2.5
	Rel	727	134	18.4	15.7	21.4	725	134	18.5	15.7	21.5	726	116	16.0	13.4	18.8
	Grade 3*Rel	727	8	1.1	0.5	2.2	725	4	0.6	0.2	1.4	726	7	1.0	0.4	2.0
	Med adv	727	1	0.1	0.0	0.8	725	6	0.8	0.3	1.8	726	1	0.1	0.0	0.8
Joint pain	All	727	103	14.2	11.7	16.9	725	95	13.1	10.7	15.8	726	81	11.2	9.0	13.7
	Grade 2*3	727	26	3.6	2.3	5.2	725	25	3.4	2.2	5.0	726	17	2.3	1.4	3.7
	Grade 3	727	4	0.6	0.2	1.4	725	5	0.7	0.2	1.6	726	1	0.1	0.0	0.8
	Rel	727	82	11.3	9.1	13.8	725	80	11.0	8.8	13.5	726	67	9.2	7.2	11.6
	Grade 3*Rel	727	4	0.6	0.2	1.4	725	4	0.6	0.2	1.4	726	1	0.1	0.0	0.8
	Med adv	727	2	0.3	0.0	1.0	725	3	0.4	0.1	1.2	726	0	0.0	0.0	0.5
Muscle aches	All	727	222	30.5	27.2	34.0	725	194	26.8	23.6	30.1	726	193	26.6	23.4	30.0
	Grade 2*3	727	52	7.2	5.4	9.3	725	41	5.7	4.1	7.6	726	43	5.9	4.3	7.9
	Grade 3	727	6	0.8	0.3	1.8	725	5	0.7	0.2	1.6	726	9	1.2	0.6	2.3
	Rel	727	202	27.8	24.6	31.2	725	178	24.6	21.5	27.9	726	170	23.4	20.4	26.7
	Grade 3*Rel	727	5	0.7	0.2	1.6	725	4	0.6	0.2	1.4	726	8	1.1	0.5	2.2
	Med adv	727	2	0.3	0.0	1.0	725	5	0.7	0.2	1.6	726	1	0.1	0.0	0.8
Shivering	All	727	55	7.6	5.7	9.7	725	51	7.0	5.3	9.1	726	53	7.3	5.5	9.4
	Grade 2*3	727	9	1.2	0.6	2.3	725	23	3.2	2.0	4.7	726	20	2.8	1.7	4.2
	Grade 3	727	4	0.6	0.2	1.4	725	10	1.4	0.7	2.5	726	4	0.6	0.2	1.4
	Rel	727	45	6.2	4.6	8.2	725	35	4.8	3.4	6.7	726	41	5.6	4.1	7.6
	Grade 3*Rel	727	3	0.4	0.1	1.2	725	7	1.0	0.4	2.0	726	4	0.6	0.2	1.4
	Med adv	727	2	0.3	0.0	1.0	725	6	0.8	0.3	1.8	726	1	0.1	0.0	0.8
Temperature/(Axillary) (°C)	All	727	26	3.6	2.3	5.2	725	33	4.6	3.2	6.3	726	20	2.8	1.7	4.2
	[38 - ...	727	24	3.3	2.1	4.9	725	27	3.7	2.5	5.4	726	19	2.6	1.6	4.1
	[38.5 - ...	727	12	1.7	0.9	2.9	725	10	1.4	0.7	2.5	726	7	1.0	0.4	2.0
	[39 - ...	727	5	0.7	0.2	1.6	725	8	1.1	0.5	2.2	726	2	0.3	0.0	1.0
	[39.6 - ...	727	3	0.4	0.1	1.2	725	4	0.6	0.2	1.4	726	0	0.0	0.0	0.5
	[40.1 - ...	727	1	0.1	0.0	0.8	725	2	0.3	0.0	1.0	726	0	0.0	0.0	0.5
	Rel	727	16	2.2	1.3	3.5	725	18	2.5	1.5	3.9	726	13	1.8	1.0	3.0
	[39 - ...*Rel	727	4	0.6	0.2	1.4	725	7	1.0	0.4	2.0	726	1	0.1	0.0	0.8
	[40.1 - ...*Rel	727	1	0.1	0.0	0.8	725	2	0.3	0.0	1.0	726	0	0.0	0.0	0.5
	Med adv	727	4	0.6	0.2	1.4	725	5	0.7	0.2	1.6	726	3	0.4	0.1	1.2

		Total				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1						
Fatigue	All	2176	499	22.9	21.2	24.8
	Grade 2*3	2176	133	6.1	5.1	7.2
	Grade 3	2176	25	1.1	0.7	1.7
	Rel	2176	403	18.5	16.9	20.2
	Grade 3*Rel	2176	18	0.8	0.5	1.3
	Med adv	2176	11	0.5	0.3	0.9
Gastrointestinal	All	2176	205	9.4	8.2	10.7
	Grade 2*3	2176	66	3.0	2.4	3.8
	Grade 3	2176	19	0.9	0.5	1.4
	Rel	2176	120	5.5	4.6	6.6
	Grade 3*Rel	2176	12	0.6	0.3	1.0
	Med adv	2176	7	0.3	0.1	0.7
Headache	All	2176	466	21.4	19.7	23.2
	Grade 2*3	2176	112	5.1	4.3	6.2
	Grade 3	2176	23	1.1	0.7	1.6
	Rel	2176	354	16.3	14.7	17.9
	Grade 3*Rel	2176	17	0.8	0.5	1.2
	Med adv	2176	8	0.4	0.2	0.7
Joint pain	All	2176	256	11.8	10.4	13.2
	Grade 2*3	2176	63	2.9	2.2	3.7
	Grade 3	2176	8	0.4	0.2	0.7
	Rel	2176	210	9.7	8.4	11.0
	Grade 3*Rel	2176	7	0.3	0.1	0.7
	Med adv	2176	5	0.2	0.1	0.5
Muscle aches	All	2176	566	26.0	24.2	27.9
	Grade 2*3	2176	124	5.7	4.8	6.8
	Grade 3	2176	16	0.7	0.4	1.2
	Rel	2176	508	23.3	21.6	25.2
	Grade 3*Rel	2176	13	0.6	0.3	1.0
	Med adv	2176	7	0.3	0.1	0.7
Shivering	All	2176	151	6.9	5.9	8.1
	Grade 2*3	2176	46	2.1	1.6	2.8
	Grade 3	2176	16	0.7	0.4	1.2
	Rel	2176	118	5.4	4.5	6.5
	Grade 3*Rel	2176	13	0.6	0.3	1.0
	Med adv	2176	9	0.4	0.2	0.8
Temperature/(Axillary) (°C)	All	2176	67	3.1	2.4	3.9
	[38 - ...	2176	58	2.7	2.0	3.4
	[38.5 - ...	2176	23	1.1	0.7	1.6
	[39 - ...	2176	14	0.6	0.4	1.1
	[39.6 - ...	2176	6	0.3	0.1	0.6
	[40.1 - ...	2176	3	0.1	0.0	0.4
	Rel	2176	41	1.9	1.4	2.5
	[39 - ...*Rel	2176	11	0.5	0.3	0.9
	[40.1 - ...*Rel	2176	3	0.1	0.0	0.4
	Med adv	2176	11	0.5	0.3	0.9
Dose 2						
Fatigue	All	563	65	11.5	9.0	14.5
	Grade 2*3	563	13	2.3	1.2	3.9
	Grade 3	563	2	0.4	0.0	1.3
	Rel	563	59	10.5	8.1	13.3

		Total				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3*Rel	563	2	0.4	0.0	1.3
	Med adv	563	0	0.0	0.0	0.7
Gastrointestinal	All	563	42	7.5	5.4	10.0
	Grade 2*3	563	13	2.3	1.2	3.9
	Grade 3	563	4	0.7	0.2	1.8
	Rel	563	29	5.2	3.5	7.3
	Grade 3*Rel	563	3	0.5	0.1	1.5
	Med adv	563	2	0.4	0.0	1.3
Headache	All	563	56	9.9	7.6	12.7
	Grade 2*3	563	14	2.5	1.4	4.1
	Grade 3	563	4	0.7	0.2	1.8
	Rel	563	49	8.7	6.5	11.3
	Grade 3*Rel	563	2	0.4	0.0	1.3
	Med adv	563	0	0.0	0.0	0.7
Joint pain	All	563	44	7.8	5.7	10.3
	Grade 2*3	563	8	1.4	0.6	2.8
	Grade 3	563	2	0.4	0.0	1.3
	Rel	563	39	6.9	5.0	9.3
	Grade 3*Rel	563	2	0.4	0.0	1.3
	Med adv	563	0	0.0	0.0	0.7
Muscle aches	All	563	101	17.9	14.9	21.4
	Grade 2*3	563	20	3.6	2.2	5.4
	Grade 3	563	4	0.7	0.2	1.8
	Rel	563	89	15.8	12.9	19.1
	Grade 3*Rel	563	4	0.7	0.2	1.8
	Med adv	563	1	0.2	0.0	1.0
Shivering	All	563	13	2.3	1.2	3.9
	Grade 2*3	563	7	1.2	0.5	2.5
	Grade 3	563	2	0.4	0.0	1.3
	Rel	563	8	1.4	0.6	2.8
	Grade 3*Rel	563	1	0.2	0.0	1.0
	Med adv	563	0	0.0	0.0	0.7
Temperature/(Axillary) (°C)	All	563	13	2.3	1.2	3.9
	[38 - ...	563	13	2.3	1.2	3.9
	[38.5 - ...	563	6	1.1	0.4	2.3
	[39 - ...	563	1	0.2	0.0	1.0
	[39.6 - ...	563	1	0.2	0.0	1.0
	[40.1 - ...	563	0	0.0	0.0	0.7
	Rel	563	7	1.2	0.5	2.5
	[39 - ...*Rel	563	1	0.2	0.0	1.0
	[40.1 - ...*Rel	563	0	0.0	0.0	0.7
	Med adv	563	1	0.2	0.0	1.0
Overall/dose						
Fatigue	All	2739	564	20.6	19.1	22.2
	Grade 2*3	2739	146	5.3	4.5	6.2
	Grade 3	2739	27	1.0	0.7	1.4
	Rel	2739	462	16.9	15.5	18.3
	Grade 3*Rel	2739	20	0.7	0.4	1.1
	Med adv	2739	11	0.4	0.2	0.7
Gastrointestinal	All	2739	247	9.0	8.0	10.2
	Grade 2*3	2739	79	2.9	2.3	3.6
	Grade 3	2739	23	0.8	0.5	1.3

		Total				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
	Rel	2739	149	5.4	4.6	6.4
	Grade 3*Rel	2739	15	0.5	0.3	0.9
	Med adv	2739	9	0.3	0.2	0.6
Headache	All	2739	522	19.1	17.6	20.6
	Grade 2*3	2739	126	4.6	3.8	5.5
	Grade 3	2739	27	1.0	0.7	1.4
	Rel	2739	403	14.7	13.4	16.1
	Grade 3*Rel	2739	19	0.7	0.4	1.1
	Med adv	2739	8	0.3	0.1	0.6
Joint pain	All	2739	300	11.0	9.8	12.2
	Grade 2*3	2739	71	2.6	2.0	3.3
	Grade 3	2739	10	0.4	0.2	0.7
	Rel	2739	249	9.1	8.0	10.2
	Grade 3*Rel	2739	9	0.3	0.2	0.6
	Med adv	2739	5	0.2	0.1	0.4
Muscle aches	All	2739	667	24.4	22.8	26.0
	Grade 2*3	2739	144	5.3	4.5	6.2
	Grade 3	2739	20	0.7	0.4	1.1
	Rel	2739	597	21.8	20.3	23.4
	Grade 3*Rel	2739	17	0.6	0.4	1.0
	Med adv	2739	8	0.3	0.1	0.6
Shivering	All	2739	164	6.0	5.1	6.9
	Grade 2*3	2739	53	1.9	1.5	2.5
	Grade 3	2739	18	0.7	0.4	1.0
	Rel	2739	126	4.6	3.8	5.5
	Grade 3*Rel	2739	14	0.5	0.3	0.9
	Med adv	2739	9	0.3	0.2	0.6
Temperature/(Axillary) (°C)	All	2739	80	2.9	2.3	3.6
	[38 - ...	2739	71	2.6	2.0	3.3
	[38.5 - ...	2739	29	1.1	0.7	1.5
	[39 - ...	2739	15	0.5	0.3	0.9
	[39.6 - ...	2739	7	0.3	0.1	0.5
	[40.1 - ...	2739	3	0.1	0.0	0.3
	Rel	2739	48	1.8	1.3	2.3
	[39 - ...*Rel	2739	12	0.4	0.2	0.8
	[40.1 - ...*Rel	2739	3	0.1	0.0	0.3
	Med adv	2739	12	0.4	0.2	0.8
Overall/subject						
Fatigue	All	2178	527	24.2	22.4	26.1
	Grade 2*3	2178	143	6.6	5.6	7.7
	Grade 3	2178	27	1.2	0.8	1.8
	Rel	2178	426	19.6	17.9	21.3
	Grade 3*Rel	2178	20	0.9	0.6	1.4
	Med adv	2178	11	0.5	0.3	0.9
Gastrointestinal	All	2178	234	10.7	9.5	12.1
	Grade 2*3	2178	77	3.5	2.8	4.4
	Grade 3	2178	23	1.1	0.7	1.6
	Rel	2178	143	6.6	5.6	7.7
	Grade 3*Rel	2178	15	0.7	0.4	1.1
	Med adv	2178	9	0.4	0.2	0.8

		Total				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
Headache	All	2178	498	22.9	21.1	24.7
	Grade 2*3	2178	125	5.7	4.8	6.8
	Grade 3	2178	27	1.2	0.8	1.8
	Rel	2178	384	17.6	16.1	19.3
	Grade 3*Rel	2178	19	0.9	0.5	1.4
	Med adv	2178	8	0.4	0.2	0.7
Joint pain	All	2178	279	12.8	11.4	14.3
	Grade 2*3	2178	68	3.1	2.4	3.9
	Grade 3	2178	10	0.5	0.2	0.8
	Rel	2178	229	10.5	9.3	11.9
	Grade 3*Rel	2178	9	0.4	0.2	0.8
	Med adv	2178	5	0.2	0.1	0.5
Muscle aches	All	2178	609	28.0	26.1	29.9
	Grade 2*3	2178	136	6.2	5.3	7.3
	Grade 3	2178	20	0.9	0.6	1.4
	Rel	2178	550	25.3	23.4	27.1
	Grade 3*Rel	2178	17	0.8	0.5	1.2
	Med adv	2178	8	0.4	0.2	0.7
Shivering	All	2178	159	7.3	6.2	8.5
	Grade 2*3	2178	52	2.4	1.8	3.1
	Grade 3	2178	18	0.8	0.5	1.3
	Rel	2178	121	5.6	4.6	6.6
	Grade 3*Rel	2178	14	0.6	0.4	1.1
	Med adv	2178	9	0.4	0.2	0.8
Temperature/(Axillary) (°C)	All	2178	79	3.6	2.9	4.5
	[38 - ...	2178	70	3.2	2.5	4.0
	[38.5 - ...	2178	29	1.3	0.9	1.9
	[39 - ...	2178	15	0.7	0.4	1.1
	[39.6 - ...	2178	7	0.3	0.1	0.7
	[40.1 - ...	2178	3	0.1	0.0	0.4
	Rel	2178	47	2.2	1.6	2.9
	[39 - ...*Rel	2178	12	0.6	0.3	1.0
	[40.1 - ...*Rel	2178	3	0.1	0.0	0.4
	Med adv	2178	12	0.6	0.3	1.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

8.2.4. Unsolicited adverse events

In addition to the solicited adverse events reported, any other adverse events that were reported to the investigator during the active phase (i.e. within the 28-day period

following vaccination) and the extended safety follow up period (180 days) were documented as unsolicited adverse events.

The global summaries of unsolicited AEs reported within the 28-day post vaccination period are presented in Table 43 (all grades) and in Table 44 (grade 3).

The global summaries of unsolicited AEs reported within the 28-day post vaccination period are presented in Supplement 65 (all grades with causal relationship to vaccination) and in Supplement 66 (grade 3 with causal relationship to vaccination).

The percentages of subjects parent(s)/LAR(s) reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and preferred term within the 28-day post vaccination period are presented in Table 45 (percentage of subjects, all grades), and in Supplement 67 (percentage of subjects, grade 3).

The percentages of subjects' parent(s)/LAR(s) reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and preferred term within the 28-day post vaccination period:

All grades with causal relationship to vaccination are presented in Supplement 68.

Grade 3 symptoms with causal relationship to vaccination are presented in Supplement 69.

For subjects 3 to 17 years old:

283 subjects (30.4%) from the Q-QIV group, 291 (31.3%) from the TIV-VB group and 275 (29.5%) from the TIV-YB group reported at least one unsolicited AE during the 28-day post-vaccination period (Table 43). Cough (5.7%, 4.1%, and 5.3%) and nasopharyngitis (5.2%, 5.1%, and 4.6%) were the most frequently reported unsolicited AEs (Table 45). Grade 3 unsolicited AEs were reported as follows: 40 subjects (4.3%) from the Q-QIV group, 41 subjects (4.4%) from the TIV-VB group, and 35 subjects (3.8%) from the TIV-YB group (Table 44 and Supplement 67).

44 subjects (4.7%) from the Q-QIV group, 47 (5.1%) from the TIV-VB group, and 44 (4.7%) from the TIV-YB group reported at least one unsolicited AE considered as related to vaccination during the 28-day post-vaccination period (Supplement 68).

7 subjects (0.8%) from the Q-QIV group, 5 (0.5%) from the TIV-VB group, and 3 (0.3%) from the TIV-YB group reported at least one grade 3 unsolicited AEs considered as related to vaccination during the 28-day post-vaccination period (Supplement 69).

For subjects 6 to 35 months old receiving Q-QIV (QIV2 group):

160 subjects (53.2%) in the QIV2 group reported at least one unsolicited AE during the 28-day post-vaccination period. Cough was the most frequently reported AE (11.3%) (Table 45). 24 subjects (8.0%) reported at least one grade 3 unsolicited AE (Table 44).

43 subjects (14.3%) from the QIV2 group reported at least one unsolicited AEs considered as related to vaccination during the 28-day post-vaccination period (Supplement 68).

4 subjects (1.3%) from the QIV2 group reported at least one grade 3 unsolicited AEs considered as related to vaccination during the 28-day post-vaccination period (Supplement 69).

Table 43 Global Summary of unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (TVC)

	Group				
	QIV1	**TIV-VB**	**TIV-YB**	**QIV2**	**Total**
Number of subjects with at least one unsolicited symptom reported	283	291	275	160	1009
Number of doses followed by at least one unsolicited symptom	329	338	319	203	1189
Number of unsolicited symptoms classified by MedDRA Preferred Term*	508	489	465	355	1817
Number of unsolicited symptoms reported	520	503	473	366	1862

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once

Table 44 Global Summary of grade 3 unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (TVC)

	Group				
	QIV1	**TIV-VB**	**TIV-YB**	**QIV2**	**Total**
Number of subjects with at least one unsolicited symptom reported	40	41	35	24	140
Number of doses followed by at least one unsolicited symptom	43	45	35	27	150
Number of unsolicited symptoms classified by MedDRA Preferred Term*	57	53	45	32	187
Number of unsolicited symptoms reported	57	53	45	32	187

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once

Table 45 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (TVC)

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		283	30.4	27.4	33.4	291	31.3	28.4	34.4	275	29.5	26.6	32.5	160	53.2	47.3	58.9
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Lymphadenopathy (10025197)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Neutropenia (10029354)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Congenital, familial and genetic disorders (10010331)	Keratosis follicular (10023369)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Stickler's syndrome (10063402)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Vitello-intestinal duct remnant (10066969)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Von willebrand's disease (10047715)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Ear pain (10014020)	3	0.3	0.1	0.9	5	0.5	0.2	1.3	5	0.5	0.2	1.2	1	0.3	0.0	1.8
	Middle ear effusion (10062545)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Otorrhoea (10033101)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tympanic membrane hyperaemia (10052154)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Eye disorders (10015919)	Conjunctivitis (10010741)	6	0.6	0.2	1.4	2	0.2	0.0	0.8	4	0.4	0.1	1.1	5	1.7	0.5	3.8
	Dark circles under eyes (10064729)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Eye inflammation (10015943)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Eye irritation (10015946)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eye movement disorder (10061129)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eye pain (10015958)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Lacrimation increased (10023644)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Myopia (10028651)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Ocular discomfort (10052143)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Ocular hyperaemia (10030041)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Refraction disorder (10038264)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Retinal degeneration (10038845)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Visual impairment (10047571)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Gastrointestinal disorders (10017947)	Abdominal discomfort (10000059)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Abdominal pain (10000081)	8	0.9	0.4	1.7	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Abdominal pain upper (10000087)	7	0.8	0.3	1.5	7	0.8	0.3	1.5	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Abnormal faeces (10000133)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Anal fissure (10002153)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Cheilitis (10008417)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Colitis (10009887)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Constipation (10010774)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	3	0.3	0.1	0.9	3	1.0	0.2	2.9
	Dental caries (10012318)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Diarrhoea (10012735)	11	1.2	0.6	2.1	10	1.1	0.5	2.0	7	0.8	0.3	1.5	20	6.6	4.1	10.1
	Dyspepsia (10013946)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Enteritis (10014866)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Flatulence (10016766)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Food poisoning (10016952)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Gastritis (10017853)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Gastrointestinal disorder (10017944)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Gastrooesophageal reflux disease (10017885)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Gingivitis (10018292)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nausea (10028813)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	7	0.8	0.3	1.5	1	0.3	0.0	1.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Odynophagia (10030094)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Stomatitis (10042128)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Teething (10043183)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	14	4.7	2.6	7.7
	Toothache (10044055)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Vomiting (10047700)	16	1.7	1.0	2.8	16	1.7	1.0	2.8	18	1.9	1.1	3.0	17	5.6	3.3	8.9
General disorders and administration site conditions (10018065)	Adverse drug reaction (10061623)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Axillary pain (10048750)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Chest pain (10008479)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Chills (10008531)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Fatigue (10016256)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	2	0.2	0.0	0.8	2	0.7	0.1	2.4
	Influenza like illness (10022004)	2	0.2	0.0	0.8	4	0.4	0.1	1.1	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Injection site anaesthesia (10022046)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site haematoma (10022066)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	3	0.3	0.1	0.9	2	0.7	0.1	2.4
	Injection site induration (10022075)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site pruritus (10022093)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site rash (10022094)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Injection site reaction (10022095)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Injection site urticaria (10022107)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site vesicles (10022111)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site warmth (10022112)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Irritability (10022998)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Malaise (10025482)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Mass (10026865)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Medical device complication (10057281)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Oedema peripheral (10030124)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Pain (10033371)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Pyrexia (10037660)	19	2.0	1.2	3.2	16	1.7	1.0	2.8	13	1.4	0.7	2.4	21	7.0	4.4	10.5
	Vaccination site pain (10068879)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Hepatobiliary disorders (10019805)	Biliary dyskinesia (10056529)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Immune system disorders (10021428)	Drug hypersensitivity (10013700)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Food allergy (10016946)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Hypersensitivity (10020751)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Multiple allergies (10028164)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Seasonal allergy (10048908)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Selective iga immunodeficiency (10039915)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Infections and infestations (10021881)	Abscess (10000269)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Acarodermatitis (10063409)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Acute sinusitis (10001076)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Acute tonsillitis (10001093)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Bacterial infection (10060945)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Bronchitis (10006451)	10	1.1	0.5	2.0	7	0.8	0.3	1.5	4	0.4	0.1	1.1	0	0.0	0.0	1.2
	Candidiasis (10007152)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Cellulitis (10007882)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Chronic sinusitis (10009137)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Conjunctivitis infective (10010742)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Conjunctivitis viral (10010755)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Croup infectious (10011416)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	4	0.4	0.1	1.1	7	2.3	0.9	4.7
	Cystitis (10011781)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Ear infection (10014011)	3	0.3	0.1	0.9	2	0.2	0.0	0.8	5	0.5	0.2	1.2	5	1.7	0.5	3.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Enteritis infectious (10058839)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Enterobiasis (10014881)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Enterovirus infection (10014909)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Eye infection (10015929)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eyelid infection (10015988)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Folliculitis (10016936)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Fungal infection (10017533)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Gastroenteritis (10017888)	7	0.8	0.3	1.5	6	0.6	0.2	1.4	9	1.0	0.4	1.8	3	1.0	0.2	2.9
	Gastroenteritis viral (10017918)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	5	1.7	0.5	3.8
	Hand-foot-and-mouth disease (10019113)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Herpangina (10019936)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Infectious mononucleosis (10021914)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Influenza (10022000)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Laryngitis (10023874)	6	0.6	0.2	1.4	3	0.3	0.1	0.9	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Lobar pneumonia (10024738)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Localised infection (10024774)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Lower respiratory tract infection (10024968)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Mycoplasma infection (10061300)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nasopharyngitis (10028810)	48	5.2	3.8	6.8	47	5.1	3.7	6.7	43	4.6	3.4	6.2	14	4.7	2.6	7.7
	Oral candidiasis (10030963)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Oral herpes (10067152)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Otitis externa (10033072)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Otitis media (10033078)	5	0.5	0.2	1.2	5	0.5	0.2	1.3	4	0.4	0.1	1.1	12	4.0	2.1	6.9

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Otitis media acute (10033079)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	2	0.2	0.0	0.8	2	0.7	0.1	2.4
	Paronychia (10034016)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pertussis (10034738)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pharyngitis (10034835)	17	1.8	1.1	2.9	16	1.7	1.0	2.8	7	0.8	0.3	1.5	2	0.7	0.1	2.4
	Pharyngitis streptococcal (10034839)	13	1.4	0.7	2.4	5	0.5	0.2	1.3	6	0.6	0.2	1.4	2	0.7	0.1	2.4
	Pharyngotonsillitis (10049140)	5	0.5	0.2	1.2	2	0.2	0.0	0.8	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Pneumonia (10035664)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	2	0.2	0.0	0.8	2	0.7	0.1	2.4
	Respiratory syncytial virus infection (10061603)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Respiratory tract infection (10062352)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	4	0.4	0.1	1.1	0	0.0	0.0	1.2
	Rhinitis (10039083)	3	0.3	0.1	0.9	2	0.2	0.0	0.8	2	0.2	0.0	0.8	7	2.3	0.9	4.7
	Roseola (10039222)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Scarlet fever (10039587)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Sinusitis (10040753)	7	0.8	0.3	1.5	3	0.3	0.1	0.9	3	0.3	0.1	0.9	3	1.0	0.2	2.9
	Skin bacterial infection (10052891)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Streptococcal infection (10061372)	2	0.2	0.0	0.8	4	0.4	0.1	1.1	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tonsillitis (10044008)	3	0.3	0.1	0.9	6	0.6	0.2	1.4	7	0.8	0.3	1.5	0	0.0	0.0	1.2
	Tooth abscess (10044016)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tooth infection (10048762)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Upper respiratory tract infection (10046306)	36	3.9	2.7	5.3	30	3.2	2.2	4.6	33	3.5	2.4	4.9	24	8.0	5.2	11.6
	Urinary tract infection (10046571)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Urinary tract infection bacterial (10054088)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Varicella (10046980)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Viral infection (10047461)	6	0.6	0.2	1.4	7	0.8	0.3	1.5	1	0.1	0.0	0.6	7	2.3	0.9	4.7
	Viral pharyngitis (10047473)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Viral rash (10047476)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Viral rhinitis (10064948)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	2	0.7	0.1	2.4
	Vulvovaginitis (10047794)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Injury, poisoning and procedural complications (10022117)	Animal bite (10002515)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Ankle fracture (10002544)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Arthropod bite (10003399)	3	0.3	0.1	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Concussion (10010254)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Contusion (10050584)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	2	0.7	0.1	2.4
	Excoriation (10049796)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Face injury (10050392)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Facial bones fracture (10016042)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Femur fracture (10016454)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Forearm fracture (10016997)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Foreign body (10070245)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Foreign body in eye (10017012)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hand fracture (10019114)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Head injury (10019196)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Humerus fracture (10020462)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint dislocation (10023204)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint sprain (10023229)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Laceration (10023572)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	3	0.3	0.1	0.9	1	0.3	0.0	1.8
	Limb injury (10061225)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Lip injury (10055082)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Mouth injury (10049294)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Open wound (10058834)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Procedural pain (10064882)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Radius fracture (10037802)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Reaction to previous exposure to any vaccine (10066904)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Splinter (10041662)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Thermal burn (10053615)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tibia fracture (10043827)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Tooth injury (10044043)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Traumatic brain injury (10060690)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Upper limb fracture (10061394)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Wound (10052428)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Wrist fracture (10048049)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Investigations (10022891)	Body temperature increased (10005911)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Cardiac murmur (10007586)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Intraocular pressure increased (10022806)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Food intolerance (10061958)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Back pain (10003988)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Costochondritis (10011219)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint range of motion decreased (10048706)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint swelling (10023232)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Muscle spasms (10028334)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Muscular weakness (10028372)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Musculoskeletal chest pain (10050819)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Musculoskeletal pain (10028391)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Musculoskeletal stiffness (10052904)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Myalgia (10028411)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Neck pain (10028836)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pain in extremity (10033425)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Pain in jaw (10033433)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Sever's disease (10050089)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Torticollis (10044074)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Skin papilloma (10040907)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Nervous system disorders (10029205)	Aphonia (10002953)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Dizziness (10013573)	2	0.2	0.0	0.8	9	1.0	0.4	1.8	6	0.6	0.2	1.4	0	0.0	0.0	1.2
	Febrile convulsion (10016284)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Grand mal convulsion (10018659)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Headache (10019211)	18	1.9	1.1	3.0	13	1.4	0.7	2.4	7	0.8	0.3	1.5	1	0.3	0.0	1.8
	Lethargy (10024264)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Migraine (10027599)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Migraine without aura (10052787)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Presyncope (10036653)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Psychomotor hyperactivity (10037211)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Somnolence (10041349)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Syncope (10042772)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Psychiatric disorders (10037175)	Abnormal behaviour (10061422)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Affective disorder (10001443)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Anxiety (10002855)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Attention deficit/hyperactivity disorder (10003736)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Depression (10012378)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eating disorder (10014062)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Emotional disorder (10014551)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Emotional distress (10049119)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Insomnia (10022437)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Trichotillomania (10044629)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Renal and urinary disorders (10038359)	Dysuria (10013990)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Enuresis (10014928)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Micturition urgency (10027566)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Reproductive system and breast disorders (10038604)	Vulvovaginal discomfort (10047786)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Asthma (10003553)	4	0.4	0.1	1.1	6	0.6	0.2	1.4	4	0.4	0.1	1.1	3	1.0	0.2	2.9
	Asthma exercise induced (10003557)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Asthmatic crisis (10064823)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Bronchial hyperreactivity (10066091)	3	0.3	0.1	0.9	4	0.4	0.1	1.1	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Cough (10011224)	53	5.7	4.3	7.4	38	4.1	2.9	5.6	49	5.3	3.9	6.9	34	11.3	8.0	15.4
	Epistaxis (10015090)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Increased upper airway secretion (10062717)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nasal congestion (10028735)	4	0.4	0.1	1.1	6	0.6	0.2	1.4	10	1.1	0.5	2.0	4	1.3	0.4	3.4
	Nasal turbinate abnormality (10052354)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Oropharyngeal blistering (10067950)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Oropharyngeal pain (10068319)	22	2.4	1.5	3.6	27	2.9	1.9	4.2	24	2.6	1.7	3.8	1	0.3	0.0	1.8
	Productive cough (10036790)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Respiratory distress (10038687)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Respiratory tract congestion (10052251)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Rhinitis allergic (10039085)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Rhinorrhoea (10039101)	17	1.8	1.1	2.9	12	1.3	0.7	2.2	19	2.0	1.2	3.2	33	11.0	7.7	15.1
	Rhonchi (10039109)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Sinus congestion (10040742)	0	0.0	0.0	0.4	3	0.3	0.1	0.9	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Sleep apnoea syndrome (10040979)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Sneezing (10041232)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	3	1.0	0.2	2.9
	Snoring (10041235)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Wheezing (10047924)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	1	0.1	0.0	0.6	2	0.7	0.1	2.4
Skin and subcutaneous tissue disorders (10040785)	Alopecia (10001760)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Angioedema (10002424)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Blister (10005191)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Cold sweat (10009866)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Dandruff (10011859)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Dermatitis (10012431)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Dermatitis atopic (10012438)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	2	0.7	0.1	2.4
	Dermatitis contact (10012442)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Drug eruption (10013687)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eczema (10014184)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Erythema (10015150)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hyperhidrosis (10020642)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Ingrowing nail (10022013)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Piloerection (10035039)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Prurigo (10037083)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Pruritus (10037087)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Rash (10037844)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	6	0.6	0.2	1.4	7	2.3	0.9	4.7
	Skin maceration (10048625)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Skin ulcer (10040943)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Urticaria (10046735)	5	0.5	0.2	1.2	5	0.5	0.2	1.3	2	0.2	0.0	0.8	1	0.3	0.0	1.8
Social circumstances (10041244)	Exposure to communicable disease (10049711)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Surgical and medical procedures (10042613)	Abscess drainage (10000279)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Sinus operation (10062245)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Tooth extraction (10062132)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Wisdom teeth removal (10047991)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Vascular disorders (10047065)	Haematoma (10018852)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pallor (10033546)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
At least one symptom = at least one symptom reported (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

8.2.5. Medically attended adverse events (MAEs)

Supplement 70 shows the percentage of subjects in the TVC reporting occurrence of medically-attended adverse events (MAEs) by MedDRA Primary System Organ Class and Preferred Term during the entire study period.

For subjects 3 to 17 years old:

346 subjects (37.1%) from the QIV1 group, 335 (36.1%) from the TIV-VB group, and 350 (37.6%) from the TIV-YB group reported at least one MAE during the entire study period. The most frequently reported MAE was coded to the MedDRA Infections and infestations SOC and Preferred Term of 'Upper respiratory tract infection' (6.9%; 6.9%, and 8.0% for the QIV1, TIV-VB, and TIV-YB groups, respectively).

For subjects 6 to 35 months old receiving Q-QIV (QIV2 group):

147 subjects (48.8%) in the QIV2 group reported at least one MAE during the entire study period. The most frequently reported MAE was coded to the MedDRA Infections and infestations SOC and Preferred Term of 'Upper respiratory tract infection' (13.3%).

8.3. According-to-protocol cohort analysis

Since the percent of vaccinated subjects excluded from the ATP cohort for safety was less than 5% of the TVC, no complementary analysis was performed on the ATP cohort for safety.

8.4. Serious adverse events

The serious adverse event (SAE) Summary Table is presented in Section 13.1 and the SAE CIOMS reports are in Section 13.2.

8.4.1. Fatal events

No fatal events were reported during the entire study period.

8.4.2. Non-fatal events

Overall, 35 SAEs were reported in 21 subjects during the entire study period (out of a total vaccinated cohort of 3094 subjects).

For subjects 3 to 17 years old:

Three (0.3%) subjects from the Q-QIV group, 6 (0.6%) from the TIV-VB group, and 5 (0.5%) from the TIV-YB group reported 4, 12, and 9 SAEs, respectively, during the entire study period (Table 46).

Two SAEs (angioedema and conjunctivitis), with onset on the day of vaccination, reported for one subject (PID (b) (6), a 12-year old male subject) in the TIV-YB group, were considered by the investigator to be related to the study vaccination. Both SAEs were reported to have recovered/resolved (Table 47).

For subjects 6 to 35 months old receiving Q-QIV (QIV2 group):

Seven (2.3%) subjects reported 10 SAEs during the entire study period (Table 46).

Two SAEs reported in the QIV2 group were considered by the investigator to be related to the study vaccination. Both SAEs (grand mal convulsion in PID (b) (6) a 1-year old female subject with onset on the day of vaccination; febrile convulsion in PID (b) (6), a 2-year old male subject with onset 18 days after vaccination) were reported to have recovered/resolved (Table 47).

Table 46 provides an analysis of all SAEs, on a per subject basis, by MedDRA Preferred Term (PT) and Primary System Organ Class (SOC).

Additional details on each of the SAEs are provided in the SAE Summary Table in Section 13.1, Table 51.

Table 46 Percentage of subjects reporting the occurrence of Serious Adverse Events (SAEs) classified by MedDRA primary System Organ Class and Preferred Term during the entire study period (TVC)

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		3	0.3	0.1	0.9	6	0.6	0.2	1.4	5	0.5	0.2	1.2	7	2.3	0.9	4.7
Blood and lymphatic system disorders (10005329)	Lymphadenitis (10025188)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Congenital, familial and genetic disorders (10010331)	Vitello-intestinal duct remnant (10066969)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Eye disorders (10015919)	Conjunctivitis (10010741)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Hepatobiliary disorders (10019805)	Biliary dyskinesia (10056529)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Immune system disorders (10021428)	Anaphylactic reaction (10002198)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hypersensitivity (10020751)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Infections and infestations (10021881)	Bronchopneumonia (10006469)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gastroenteritis (10017888)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Influenza (10022000)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Lobar pneumonia (10024738)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pneumonia (10035664)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pneumonia viral (10035737)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Respiratory syncytial virus infection (10061603)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Injury, poisoning and procedural complications (10022117)	Accidental overdose (10000381)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Facial bones fracture (10016042)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Foreign body (10070245)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Head injury (10019196)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Joint dislocation (10023204)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Traumatic brain injury (10060690)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Metabolism and nutrition disorders (10027433)	Hypovolaemia (10021137)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Grand mal convulsion (10018659)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Psychiatric disorders (10037175)	Anxiety (10002855)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Depression (10012378)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Suicidal ideation (10042458)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	3	1.0	0.2	2.9
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Urticaria (10046735)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Vascular disorders (10047065)	Hypertension (10020772)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
At least one symptom = at least one symptom reported (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting at least once the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 47 Listing of SAEs considered by the study investigator to be related to vaccination and reported during the entire study period (TVC)

Group	Sub. No.	Case Id	Age at onset (Year)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
TIV-YB	(b) (6)		12	M	Angioedema	Angioedema	Skin and subcutaneous tissue disorders	MD	1	0	7	2	Y	Recovered/resolved
					Acute conjunctivitis	Conjunctivitis	Eye disorders	MD	1	0	7	1	Y	Recovered/resolved
QIV2	(b) (6)		1	F	Grand mal seizure	Grand mal convulsion	Nervous system disorders	ER	1	0	1	3	Y	Recovered/resolved
	(b) (6)		2	M	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	18	1	3	Y	Recovered/resolved

8.5. Adverse events leading to premature discontinuation of study vaccine and/or study

One subject (PID (b) (6) from the QIV2 group (FLU Q-QIV/6-35 months of age) was withdrawn (no Day 180 contact) subsequent to a non-serious adverse event (moderate fever) which was reported as "resolved/recovered." The decision to withdraw from the study was made by the subject's parent(s)/legally acceptable representative(s).

8.6. Other significant adverse events

8.6.1. Potential Immune-Mediated Diseases (pIMDs)

No pIMDs were reported in QIV1 and QIV2 groups. There were two reported cases of pIMDs during the entire study period, one each in the TIV-VB (Vitiligo) and TIV-YB (Psoriasis) groups. The details of each pIMD are presented in Table 48. Neither of the two pIMDs was considered by the investigator to be causally related to vaccination and both were reported as 'not recovered/not resolved'at the end of the study.

Table 48 Listing of potential Immune-Mediated Diseases (pIMDs) reported during the entire study period (All enrolled subjects)

Group	Sub. No.	Age at onset (Year)	Sex	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Intensity	Causality	Outcome	Serious
TIV-VB	(b) (6)	7	F	Vitiligo	Skin and subcutaneous tissue disorders	N	2	120	.	1	N	Not recovered/ not resolved	N
TIV-YB	(b) (6)	4	M	Psoriasis	Skin and subcutaneous tissue disorders	N	2	104	.	2	N	Not recovered/ not resolved	N

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victotria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
NOGRP = No assigned group
MA = Medical Advice

8.7. Concomitant medications and vaccinations

Table 49 shows the incidence of concomitant vaccination during the entire study period.

Table 50 shows the incidence of concomitant medication during the 28-day (Days 0-27) post-vaccination period.

For subjects 3 to 17 years old:

- Concomitant medications were taken by 35.8%, 32.9%, and 31.5% of subjects in the QIV1, TIV-VB, and TIV-YB groups, respectively.

- Prophylactic antipyretic medications, taken in anticipation of adverse events, were used by 0.3%, 0.5%, and 0.0% of subjects in the QIV1, TIV-VB, and TIV-YB groups, respectively, during the entire study period (Table 50).

For subjects 6 to 35 months old receiving Q-QIV (QIV2 group):

- Concomitant medications and prophylactic antipyretic medications were taken by 50.5% and 2.3% of subjects, respectively.

Table 49 Incidence of concomitant vaccination during the entire study period (TVC)

					95%CI	
Concomitant Vaccination	**Group**	**N**	**n**	**%**	**LL**	**UL**
ACTHIB	QIV2	301	1	0.33	0.0	1.8
ADACEL	QIV1	932	2	0.21	0.0	0.8
	TIV-YB	932	1	0.11	0.0	0.6
ADACEL (TDAP)	QIV1	932	1	0.11	0.0	0.6
ALTENARIA VACCINE	TIV-YB	932	1	0.11	0.0	0.6
BOOSTRIX VACCINE	TIV-YB	932	1	0.11	0.0	0.6
CERVARIX	TIV-VB	929	1	0.11	0.0	0.6
CHICKEN POX	QIV2	301	2	0.66	0.1	2.4
COMMERCIAL FLU VACCINE	QIV1	932	3	0.32	0.1	0.9
DAPTACEL	TIV-YB	932	2	0.21	0.0	0.8
	QIV2	301	1	0.33	0.0	1.8
DEPIGOID	TIV-VB	929	1	0.11	0.0	0.6
DEPIGOID DERMATOPHAGOIDES PTERONYSSINUS	QIV1	932	3	0.32	0.1	0.9
DEPIGOID GRAMINEAS-OLIVO	TIV-VB	929	2	0.22	0.0	0.8
DEPIGOID LETI	TIV-YB	932	2	0.21	0.0	0.8
DIPHTHERIA / PERTUSSIS / TETANUS	TIV-YB	932	1	0.11	0.0	0.6
DIPHTHERIA TETANUS PERTUSSIS	TIV-YB	932	1	0.11	0.0	0.6
DIPHTHERIA, PERTUSSIS, TETANUS	QIV1	932	9	0.97	0.4	1.8
	TIV-VB	929	5	0.54	0.2	1.3
	TIV-YB	932	4	0.43	0.1	1.1
DIPHTHERIA, PERTUSSIS, TETANUS, HEPATITIS B, HIB	TIV-VB	929	1	0.11	0.0	0.6
DIPHTHERIA, PERTUSSIS,TETANUS	TIV-YB	932	1	0.11	0.0	0.6

					95%CI	
Concomitant Vaccination	**Group**	**N**	**n**	**%**	**LL**	**UL**
DIPHTHERIA,PERTUSSIS, TETANUS	QIV1	932	1	0.11	0.0	0.6
DIPHTHERIA-TETANUS VACCINE	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	2	0.22	0.0	0.8
DIPHTHERIA. PERTUSSIS, TETANUS	QIV1	932	1	0.11	0.0	0.6
DIPTHERIA, TETANUS, PERTUSSIS	TIV-VB	929	1	0.11	0.0	0.6
DPTP	QIV2	301	1	0.33	0.0	1.8
DPTP/HIB	QIV2	301	1	0.33	0.0	1.8
DT ADULTOS (AVENTIS PASTEUR)	TIV-VB	929	1	0.11	0.0	0.6
DTAP	QIV1	932	5	0.54	0.2	1.2
	TIV-VB	929	4	0.43	0.1	1.1
	TIV-YB	932	8	0.86	0.4	1.7
	QIV2	301	11	3.65	1.8	6.4
DTAP #4	QIV2	301	1	0.33	0.0	1.8
DTAP (KINRIX)	TIV-YB	932	1	0.11	0.0	0.6
DTAP DT	TIV-YB	932	1	0.11	0.0	0.6
DTAP VACCINE	QIV2	301	1	0.33	0.0	1.8
DTPA	QIV1	932	3	0.32	0.1	0.9
	TIV-VB	929	5	0.54	0.2	1.3
	TIV-YB	932	3	0.32	0.1	0.9
DTPA VACCINE	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	2	0.21	0.0	0.8
ENGERIX-B	TIV-YB	932	1	0.11	0.0	0.6
GARASIL	QIV1	932	1	0.11	0.0	0.6
GARDASIL	QIV1	932	10	1.07	0.5	2.0
	TIV-VB	929	4	0.43	0.1	1.1
	TIV-YB	932	1	0.11	0.0	0.6
GARDASIL VACCINATION	QIV1	932	1	0.11	0.0	0.6
GARDISIL (HPV)	QIV1	932	1	0.11	0.0	0.6
HAEMOPHILUS INFLUENZAE TYPE B	TIV-VB	929	1	0.11	0.0	0.6
	QIV2	301	1	0.33	0.0	1.8
HAEMPOPHILUS TYPE B	QIV2	301	1	0.33	0.0	1.8
HAPATITIS A	QIV1	932	1	0.11	0.0	0.6
HAV	QIV2	301	3	1.00	0.2	2.9
HAV #2	QIV2	301	1	0.33	0.0	1.8
HAVRIX	QIV1	932	20	2.15	1.3	3.3
	TIV-VB	929	20	2.15	1.3	3.3
	TIV-YB	932	29	3.11	2.1	4.4
	QIV2	301	6	1.99	0.7	4.3
HBV	QIV2	301	1	0.33	0.0	1.8
HBV3	QIV2	301	1	0.33	0.0	1.8
HEP A	TIV-VB	929	1	0.11	0.0	0.6
	QIV2	301	4	1.33	0.4	3.4
HEP A 2	TIV-YB	932	1	0.11	0.0	0.6
HEP A/PEDI/ADOL	QIV2	301	1	0.33	0.0	1.8
HEP B	QIV2	301	1	0.33	0.0	1.8
HEPA	QIV2	301	1	0.33	0.0	1.8
HEPA (HAVRIX)	QIV2	301	1	0.33	0.0	1.8
HEPATITIS A	QIV1	932	4	0.43	0.1	1.1
	TIV-VB	929	3	0.32	0.1	0.9
	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	9	2.99	1.4	5.6

					95%CI	
Concomitant Vaccination	**Group**	**N**	**n**	**%**	**LL**	**UL**
HEPATITIS A BOOSTER	QIV2	301	1	0.33	0.0	1.8
HEPATITIS A VACCINATION	TIV-YB	932	1	0.11	0.0	0.6
HEPATITIS A VACCINE	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	4	0.43	0.1	1.1
	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	3	1.00	0.2	2.9
HEPATITIS B	QIV1	932	2	0.21	0.0	0.8
	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	3	0.32	0.1	0.9
	QIV2	301	4	1.33	0.4	3.4
HEPATITIS B VACCINE	TIV-VB	929	2	0.22	0.0	0.8
	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	1	0.33	0.0	1.8
HEPATITS A	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	1	0.11	0.0	0.6
	QIV2	301	1	0.33	0.0	1.8
HIB	QIV1	932	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	15	4.98	2.8	8.1
HIB #4	QIV2	301	1	0.33	0.0	1.8
HIB VACCINE	TIV-VB	929	1	0.11	0.0	0.6
	QIV2	301	1	0.33	0.0	1.8
HPV	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	3	0.32	0.1	0.9
HPV #2	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
HPV 2	TIV-VB	929	1	0.11	0.0	0.6
HPV VACCINE	QIV1	932	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
HPV3	QIV1	932	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
HUMAN PAPILLOMA VIRUS	TIV-YB	932	1	0.11	0.0	0.6
HUMAN VIRUS PAPILOMA	TIV-YB	932	1	0.11	0.0	0.6
INFANRIX VACCINE	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
INFLUENZA	QIV1	932	2	0.21	0.0	0.8
INFLUENZA VACCINE	QIV2	301	1	0.33	0.0	1.8
INMUNOTHERAPY FOR GRASS AND OLIVES	TIV-YB	932	1	0.11	0.0	0.6
IPOL	TIV-YB	932	2	0.21	0.0	0.8
IPV	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	2	0.22	0.0	0.8
	TIV-YB	932	5	0.54	0.2	1.2
IPV/OPV (KINRIX)	TIV-YB	932	1	0.11	0.0	0.6
KINRIX	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
KINRIX (DTAP, IPV) VACCINE	QIV1	932	1	0.11	0.0	0.6
KINRIX VACCINE (DTAP, POLIO)	TIV-VB	929	1	0.11	0.0	0.6
MCV4	QIV1	932	1	0.11	0.0	0.6
MEASLES MUMPS RUBELLA	QIV2	301	2	0.66	0.1	2.4
MEASLES, MUMPS AND RUBELLA VACCINE	TIV-YB	932	1	0.11	0.0	0.6

					95%CI	
Concomitant Vaccination	**Group**	**N**	**n**	**%**	**LL**	**UL**
MEASLES, MUMPS, RUBELLA VACCINE	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	1	0.11	0.0	0.6
	QIV2	301	2	0.66	0.1	2.4
MEASLES, RUBELLA	TIV-VB	929	2	0.22	0.0	0.8
MEASLES, RUBELLA, MUMPS	TIV-VB	929	2	0.22	0.0	0.8
MEASLES, RUBELLA,MUMPS	TIV-VB	929	2	0.22	0.0	0.8
MEASLES,MUMPS, RUBEOLLA	TIV-YB	932	1	0.11	0.0	0.6
MEASLES/MUMPS/RUBELLA	QIV2	301	1	0.33	0.0	1.8
MEN C CONJ	TIV-YB	932	1	0.11	0.0	0.6
MEN-C	QIV2	301	1	0.33	0.0	1.8
MENACTRA	QIV1	932	2	0.21	0.0	0.8
	TIV-VB	929	2	0.22	0.0	0.8
	TIV-YB	932	2	0.21	0.0	0.8
MENACTRA (MENINGICOCCAL)	QIV1	932	1	0.11	0.0	0.6
MENC	QIV2	301	2	0.66	0.1	2.4
MENINGOCOCCAL	QIV1	932	1	0.11	0.0	0.6
MENINGOCOCCAL C CONJUGATE	QIV1	932	1	0.11	0.0	0.6
MENINGOCOCCAL VACCINE	TIV-YB	932	1	0.11	0.0	0.6
MENINGOCOCCOL VACCINE	TIV-VB	929	1	0.11	0.0	0.6
MENINGOCOCO C	QIV1	932	1	0.11	0.0	0.6
MENJUGATE	QIV2	301	6	1.99	0.7	4.3
MENVEO	QIV1	932	1	0.11	0.0	0.6
MITES AND FUNGI VACCINE MOISTURE	QIV1	932	2	0.21	0.0	0.8
MMR	QIV1	932	5	0.54	0.2	1.2
	TIV-VB	929	10	1.08	0.5	2.0
	TIV-YB	932	12	1.29	0.7	2.2
	QIV2	301	33	10.96	7.7	15.1
MMR (MERCK)	TIV-YB	932	1	0.11	0.0	0.6
MMR 2	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	4	1.33	0.4	3.4
MMR II	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	3	1.00	0.2	2.9
MMR VACCINE	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	2	0.22	0.0	0.8
	TIV-YB	932	2	0.21	0.0	0.8
MMR-II	TIV-YB	932	1	0.11	0.0	0.6
MMRVACCINE	QIV2	301	1	0.33	0.0	1.8
NEIS VAC-C	QIV2	301	1	0.33	0.0	1.8
NEISVAC-C	QIV2	301	1	0.33	0.0	1.8
PANGRAMIN DEPOT	TIV-YB	932	3	0.32	0.1	0.9
PCV 13	QIV2	301	4	1.33	0.4	3.4
PCV 13 VACCINE	QIV2	301	1	0.33	0.0	1.8
PCV 7	QIV2	301	1	0.33	0.0	1.8
PCV-13	QIV1	932	1	0.11	0.0	0.6
PCV13	QIV2	301	5	1.66	0.5	3.8
PCV7	QIV2	301	3	1.00	0.2	2.9
PEDIACEL	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	4	1.33	0.4	3.4
PENTACEL	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	22	7.31	4.6	10.9
PNEUMOCCAL	QIV1	932	1	0.11	0.0	0.6
	QIV2	301	1	0.33	0.0	1.8

					95%CI	
Concomitant Vaccination	**Group**	**N**	**n**	**%**	**LL**	**UL**
PNEUMOCOCCAL	QIV2	301	1	0.33	0.0	1.8
PNEUMOCOCCUS	TIV-VB	929	1	0.11	0.0	0.6
PNEUMOCOCCUS HEPTAVALENTE	QIV1	932	1	0.11	0.0	0.6
POLIO	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
	QIV2	301	2	0.66	0.1	2.4
POLIO 4	TIV-YB	932	1	0.11	0.0	0.6
POLIO SABIN	QIV1	932	2	0.21	0.0	0.8
	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	5	0.54	0.2	1.2
POLIO, INACTIVE	QIV1	932	1	0.11	0.0	0.6
POLIOMYELITIS	QIV1	932	5	0.54	0.2	1.2
	TIV-VB	929	8	0.86	0.4	1.7
	TIV-YB	932	5	0.54	0.2	1.2
PREVENAR 13	QIV1	932	1	0.11	0.0	0.6
	QIV2	301	1	0.33	0.0	1.8
PREVNAR	TIV-YB	932	2	0.21	0.0	0.8
	QIV2	301	15	4.98	2.8	8.1
PREVNAR 13	QIV1	932	3	0.32	0.1	0.9
	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	4	0.43	0.1	1.1
	QIV2	301	9	2.99	1.4	5.6
PREVNAR VACCINE	TIV-VB	929	1	0.11	0.0	0.6
	QIV2	301	1	0.33	0.0	1.8
PREVNAR13	QIV2	301	1	0.33	0.0	1.8
PVC7	QIV2	301	1	0.33	0.0	1.8
QUADRACEL	QIV1	932	2	0.21	0.0	0.8
RECOMBIVAX	QIV2	301	1	0.33	0.0	1.8
ROTA VIRUS	QIV2	301	1	0.33	0.0	1.8
ROTAVIRUS	QIV2	301	3	1.00	0.2	2.9
SEASONAL VACCINE	QIV2	301	1	0.33	0.0	1.8
STALORAL	TIV-VB	929	1	0.11	0.0	0.6
STALORAL 300 RAPID	QIV1	932	1	0.11	0.0	0.6
SYNFLORIX	QIV2	301	4	1.33	0.4	3.4
SYNFOLRIX	QIV2	301	1	0.33	0.0	1.8
T-DAP	QIV1	932	1	0.11	0.0	0.6
TB	TIV-YB	932	1	0.11	0.0	0.6
TD	TIV-YB	932	1	0.11	0.0	0.6
TDAP	QIV1	932	3	0.32	0.1	0.9
	TIV-YB	932	1	0.11	0.0	0.6
TDAP BOOSTER	TIV-VB	929	1	0.11	0.0	0.6
TDPA	QIV1	932	3	0.32	0.1	0.9
	TIV-VB	929	4	0.43	0.1	1.1
TETANOS VACCINE	QIV1	932	1	0.11	0.0	0.6
TETANUS	QIV1	932	1	0.11	0.0	0.6
TETANUS AND DIPTHERIA	QIV1	932	1	0.11	0.0	0.6
TETANUS, DIPHTHERIA	QIV1	932	2	0.21	0.0	0.8
	TIV-VB	929	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6
TETANUS, DIPHTHERIA, AND PERTUSSIS	TIV-YB	932	1	0.11	0.0	0.6
VAQTA	QIV1	932	1	0.11	0.0	0.6
	TIV-YB	932	1	0.11	0.0	0.6

					95%CI	
Concomitant Vaccination	**Group**	**N**	**n**	**%**	**LL**	**UL**
	QIV2	301	3	1.00	0.2	2.9
VARICELA	QIV1	932	3	0.32	0.1	0.9
	TIV-VB	929	6	0.65	0.2	1.4
	TIV-YB	932	6	0.64	0.2	1.4
VARICELE	TIV-VB	929	1	0.11	0.0	0.6
VARICELLA	QIV1	932	22	2.36	1.5	3.6
	TIV-VB	929	28	3.01	2.0	4.3
	TIV-YB	932	29	3.11	2.1	4.4
	QIV2	301	22	7.31	4.6	10.9
VARICELLA (MERCK)	TIV-YB	932	1	0.11	0.0	0.6
VARICELLA VACCINATION	TIV-VB	929	1	0.11	0.0	0.6
VARICELLA VACCINE	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	1	0.11	0.0	0.6
	QIV2	301	3	1.00	0.2	2.9
VARIVAX	QIV1	932	1	0.11	0.0	0.6
	TIV-VB	929	2	0.22	0.0	0.8
	TIV-YB	932	4	0.43	0.1	1.1
	QIV2	301	5	1.66	0.5	3.8
VARIVAX 3	QIV2	301	4	1.33	0.4	3.4
VIRUS PAPILOMA HUMANO (AVENTIS PASTEUR)	TIV-VB	929	2	0.22	0.0	0.8

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victotria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects who received the specified concomitant vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 50 Incidence of concomitant medication during the 28-day (Days 0-27) post-vaccination period by dose and overall (TVC)

	QIV1					TIV-VB					TIV-YB				
				95% CI					95% CI					95% CI	
	N	N	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1															
Any	932	291	31.2	28.3	34.3	929	266	28.6	25.7	31.7	932	246	26.4	23.6	29.4
Any antipyretic	932	161	17.3	14.9	19.9	929	153	16.5	14.1	19.0	932	122	13.1	11.0	15.4
Prophylactic antipyretic	932	2	0.2	0.0	0.8	929	5	0.5	0.2	1.3	932	0	0.0	0.0	0.4
Dose 2															
Any	331	93	28.1	23.3	33.3	330	86	26.1	21.4	31.2	328	87	26.5	21.8	31.7
Any antipyretic	331	49	14.8	11.2	19.1	330	39	11.8	8.5	15.8	328	40	12.2	8.9	16.2
Prophylactic antipyretic	331	1	0.3	0.0	1.7	330	0	0.0	0.0	1.1	328	0	0.0	0.0	1.1
Overall/dose															
Any	1263	384	30.4	27.9	33.0	1259	352	28.0	25.5	30.5	1260	333	26.4	24.0	29.0
Any antipyretic	1263	210	16.6	14.6	18.8	1259	192	15.3	13.3	17.4	1260	162	12.9	11.1	14.8
Prophylactic antipyretic	1263	3	0.2	0.0	0.7	1259	5	0.4	0.1	0.9	1260	0	0.0	0.0	0.3
Overall/subject															
Any	932	334	35.8	32.8	39.0	929	306	32.9	29.9	36.1	932	294	31.5	28.6	34.6
Any antipyretic	932	194	20.8	18.3	23.6	929	176	18.9	16.5	21.6	932	152	16.3	14.0	18.8
Prophylactic antipyretic	932	3	0.3	0.1	0.9	929	5	0.5	0.2	1.3	932	0	0.0	0.0	0.4

	QIV2				
				95% CI	
	N	n	%	LL	UL
Dose 1					
Any	301	124	41.2	35.6	47.0
Any antipyretic	301	74	24.6	19.8	29.9
Prophylactic antipyretic	301	7	2.3	0.9	4.7
Dose 2					
Any	233	70	30.0	24.2	36.4
Any antipyretic	233	45	19.3	14.4	25.0
Prophylactic antipyretic	233	1	0.4	0.0	2.4
Overall/dose					
Any	534	194	36.3	32.2	40.6
Any antipyretic	534	119	22.3	18.8	26.1
Prophylactic antipyretic	534	8	1.5	0.6	2.9
Overall/subject					
Any	301	152	50.5	44.7	56.3
Any antipyretic	301	97	32.2	27.0	37.8
Prophylactic antipyretic	301	7	2.3	0.9	4.7

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

8.8. Pregnancy

There was one case of pregnancy (PID (b) (6) reported in this study. This 17-year-old female, with a history of urinary tract infection and acne, received Fluarix-VB on (b) (6) Her last menstrual period was on 30 November 2010; the subject was exposed to vaccine prior to conception. On (b) (6) , after 38 weeks gestation, she gave birth to a live male infant by caesarian section due to failure to progress and umbilical cord wrapped around the neck of the fetus.

8.9. Safety conclusions

The secondary objectives of this study included the comparative evaluation of the reactogenicity and safety profiles of the FLU Q-QIV, *Fluarix*-VB (TIV-VB), and *Fluarix*-YB (TIV-YB) vaccines, for all subjects 3 to 17 years of age, in terms of solicited local and general symptoms, unsolicited AEs, unsolicited medically attended AEs (MAEs), pIMDs, and SAEs. The same reactogenicity and safety parameters were also evaluated for the FLU Q-QIV vaccine in subjects 6 to 35 months of age (QIV2 group).

Based on the overall results, the following conclusions can be made:

- Overall incidence of *solicited and unsolicited* adverse events (AEs) (overall/subject):
  - *Any* solicited and unsolicited AEs were reported for 77.3%, 71.6%, and 69.0% of subjects in the Q-QIV, TIV-VB, and TIV-YB groups, respectively, and for 74.8% of subjects in the QIV2 group.
- *Solicited local* AEs (overall/subject):
  - Injection site pain was the most frequently reported local AE across all treatment groups with a a lower incidence in children 6-35 months of age (reported for 69.8%, 59.0% and 59.2% of 3-17 year-old subjects in the QIV1, TIV-VB, TIV-YB and 50.3% of 6-35 month-old subjects in the QIV2 groups, respectively).
  - Grade 3 injection site pain was reported for 3.8%, 2.3%, 2.8%, and 2.0% of subjects in the QIV1, TIV-VB, TIV-YB, and QIV2 groups, respectively.
- *Solicited general* AEs (overall/subject):
  - Drowsiness (24.9%, 25.1%, and 27.0% of subjects) and irritability (31.9%, 23.5%, and 25.4% of subjects) were the most frequently reported general AEs across the three treatment groups (QIV1, TIV-VB, and TIV-YB groups, respectively) among subjects 3 to 5 years of age. In the QIV2 group (Q-QIV in subjects 6 to 35 months of age), irritability (48.3%) was the most frequently reported general AE, followed by drowsiness (34.9%), and loss of appetite (31.8%).
  - Muscle ache (30.5%, 26.8%, and 26.6% of subjects), fatigue (23.8%, 24.4%, and 24.4% of subjects), and headache (23.4%, 23.6%, and 21.6% of subjects) were the most frequently reported general AEs across the three treatment groups (Q-QIV, TIV-VB, and TIV-YB groups, respectively) in subjects 5 years of age and older.

  - Grade 3 solicited general AEs, including fever, were reported with a very low incidence rate, ranging from 0.0% to 3.2% (in subjects 3 to <5 years of age) and 0.0% to 1.8% (in subjects ≥5 to 17 years of age).

- *Unsolicited AEs and MAEs* (medically-attended adverse events):
  - Among the 3 to 17 year-old subjects, 283 (30.4%) from the QIV1 group, 291 (31.3%) from the TIV-VB group, and 275 (29.5%) from the TIV-YB group reported at least one unsolicited adverse event (AE) during the 28-day post-vaccination period. In the QIV2, 6 to 35 months old age group, 160 subjects (53.2%) reported at least one unsolicited AE during the 28-day post-vaccination period. For all treatments and across both age groups, cough was the most frequently reported AE.
  - Among the 3 to 17 year old subjects, 346 subjects (37.1%) from the QIV1 group, 335 (36.1%) from the TIV-VB group, and 350 (37.6%) from the TIV-YB group reported at least one MAE during the entire study period. In the QIV-only, 6 to 35 months old age group (QIV2), 147 subjects (48.8%) reported at least one MAE during the entire study period. For all treatments and across both age groups, upper respiratory tract infection was the most frequently reported MAE.
- *SAEs* (Serious adverse events):
- No fatal SAEs were reported during the entire study period. Overall, 35 SAEs were reported in 21 subjects during the entire study period (out of a total vaccinated cohort of 3094 subjects).
- In subjects 3-17 years of age, two SAEs (angioedema and conjunctivitis) with onset on the day of vaccination reported for one subject (PID (b) (6), a 12-year old male subject) in the *Fluarix*-YB (TIV-YB) group were considered by the investigator to be related to the study vaccination. Both SAEs were reported to have recovered/resolved.
- In subjects 6-35 months of age, two SAEs (grand mal convulsion in PID (b) (6) a 1-year old female subject with onset on the day of the first dose of Q-QIV; febrile convulsion in PID (b) (6) a 2-year old male subject with onset 18 days after first dose of Q-QIV) were also considered to be related to vaccination. Both SAEs were reported to have recovered/resolved.

9. OVERALL CONCLUSIONS

The major conclusions from the FLU-Q-QIV-003 study are summarized as follows:

- The study met its confirmatory primary objective of demonstrating immunogenic non-inferiority of the quadrivalent FLU Q-QIV vaccine compared to the trivalent *Fluarix* vaccines, TIV-VB (*Fluarix* containing Victoria B strain) or TIV-YB (*Fluarix* containing Yamagata B strain) after completion of the vaccination series in children 3 to 17 years of age.
- The study met the confirmatory secondary objective of demonstrating immunogenic superiority of the quadrivalent FLU Q-QIV vaccine over the trivalent Fluarix vaccines, TIV-VB (with respect to the Yamagata lineage B strain) and TIV-YB (with respect to the Victoria lineage B strain) after completion of the vaccination series in children 3 to 17 years of age.
- The study also achieved its confirmatory secondary objective of demonstrating that, in children 3 to 17 years of age, the immunogenic response to the alternate, Yamagata-lineage, B strain in FLU Q-QIV fulfilled CBER's immunogenicity criteria predictive of clinical benefit.
- The descriptive immunogenicity data indicated that, in children 6 to 35 months of age, each of the four strains in the FLU Q-QIV vaccine met CBER's SPR and SCR criteria indicative of clinical benefit with the exception of the SPR for the A/Victoria/210/2009 (H3N2) strain.
- Within the 7 day post-vaccination period, 77.3 %, 71.6% and 69.0% of subjects in the QIV1, TIV-VB, and TIV-YB groups (3-17 years of age), respectively, and 74.8% of subjects in the QIV2 group (6-35 months of age) reported at least one solicited or unsolicited adverse event AE).
- Within the 28 day post-vaccination period, 30.4% , 31.3%, and 29.5% of subjects in the QIV1, TIV-VB, and TIV-YB groups (3-17 years of age), respectively, and 53.2% of subjects in the QIV2 group (6-35months of age) reported at least one unsolicited adverse event.
- Within the entire study period, 37.1%, 36.1%, and 37.6% of subjects in the QIV1, TIV-VB, and TIV-YB groups (3-17 years of age), respectively, and 48.8% of subjects in the QIV2 group (6-35months of age) reported at least one medically-attended adverse event (MAE).
- No fatal serious adverse events (SAEs) were reported during the entire study period.
- Two SAEs (angioedema and conjunctivitis), reported for one subject in the TIV-YB group (3-17 years of age), were considered by the investigator to be related to the vaccination. Both SAEs were reported to have recovered/resolved.
- Two SAEs (grand mal convulsion in PID (b) (6) with onset on the day of the first dose of Q-QIV and febrile convulsion in PID (b) (6) with onset on 18 days after first dose of Q-QIV) reported in the QIV2 group (6-35 months of age) were considered by investigator to be related to the vaccination. Both SAEs were reported to have recovered/resolved.

10. SUPPLEMENTS

Supplement 1 Number of subjects by center (TVC)

	QIV1	TIV-VB	TIV-YB	QIV2	Total	
Center	n	n	n	n	n	%
80199	17	15	14	5	51	1.6
80205	10	10	10	6	36	1.2
80210	47	49	48	15	159	5.1
80217	19	17	16	7	59	1.9
80223	16	15	16	6	53	1.7
80224	12	11	11	5	39	1.3
80225	23	22	21	15	81	2.6
80227	21	19	21	7	68	2.2
80229	75	69	74	38	256	8.3
80232	52	53	54	15	174	5.6
80233	40	40	39	22	141	4.6
80235	15	14	14	3	46	1.5
80236	42	42	42	20	146	4.7
80237	37	39	38	11	125	4.0
80321	26	26	26	5	83	2.7
81081	60	60	60	0	180	5.8
81435	30	33	32	19	114	3.7
81615	104	104	106	1	315	10.2
81616	6	7	4	0	17	0.5
81617	52	53	52	0	157	5.1
81633	8	7	6	0	21	0.7
82306	34	37	36	0	107	3.5
82650	12	14	14	20	60	1.9
82651	4	3	5	7	19	0.6
82652	4	4	6	13	27	0.9
82653	19	17	19	15	70	2.3
82654	14	15	13	7	49	1.6
82655	9	9	7	5	30	1.0
82656	22	22	23	17	84	2.7
82731	65	64	65	0	194	6.3
82732	33	34	34	0	101	3.3
83422	4	5	6	17	32	1.0
All	932	929	932	301	3094	100

QIV1 = Flu Q-QIV (3 - 17 years); TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years); QIV2 = Flu Q-QIV (6 - 35 months)
n = number of subjects included in each group or in total for a given center or for all centers
All = sum of all subjects in each group or in total (sum of all groups)
% = n/All x 100
Center = GSK Biologicals assigned center number

Supplement 2 Number of subjects at each visit and list of withdrawn subjects (TVC)

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
QIV1	VISIT DAY 0	932		
			(b) (6)	PI DECISION DUE TO EXCESSIVE NO-SHOWS
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
	VISIT DAY 28	916		
			(b) (6)	LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
	VISIT DAY 56	336		
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
	ESFU(D180)	894		
TIV-VB	VISIT DAY 0	929	(b) (6)	
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
	VISIT DAY 28	919		
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
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				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
	VISIT DAY 56	328		
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
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				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
	ESFU(D180)	889		
TIV-YB	VISIT DAY 0	932		
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
	VISIT DAY 28	921		
				CLIENT UNABLE TO COME TO CENTER WITHIN WINDOW PERIOD
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
	VISIT DAY 56	325		
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
	ESFU(D180)	902		
QIV2	VISIT DAY 0	301		
				PROTOCOL VIOLATION
				PROTOCOL VIOLATION
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP*CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
	VISIT DAY 28	293		
				LOST TO FOLLOW-UP*NON SERIOUS ADVERSE EVENT

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	MIGRATED / MOVED FROM THE STUDY AREA
				LOST TO FOLLOW-UP
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				MIGRATED / MOVED FROM THE STUDY AREA
				MIGRATED / MOVED FROM THE STUDY AREA
				MIGRATED / MOVED FROM THE STUDY AREA
				LOST TO FOLLOW-UP
	VISIT DAY 56	226		
				CONSENT WITHDRAWAL, NOT DUE TO AN ADVERSE EVENT
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
				LOST TO FOLLOW-UP
	ESFU(D180)	275		

Supplement 3 Deviations from specifications for age and intervals between study visits for primed subjects (3 to 17 year old) (TVC)

		Age	Dose:1-PI(D28)	Dose:1-ESFU(D180)
Group		**Protocol**	**Protocol**	**Protocol**
		from 3 to 17 year	from 25 to 42 days	from 166 to 201 days
QIV1	N	582	574	564
	n	0	1	2
	%	0.0	0.2	0.4
	range	3 to 17	25 to 53	165 to 202
TIV-VB	N	589	577	572
	n	0	7	5
	%	0.0	1.2	0.9
	range	3 to 17	25 to 53	166 to 208
TIV-YB	N	595	583	582
	n	0	6	4
	%	0.0	1.0	0.7
	range	3 to 17	25 to 119	166 to 204

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Supplement 4 Deviations from specifications for age and intervals between study visits for unprimed subjects (3 to 17 year old) (TVC)

		Age	Dose:1-PI(D28)	Dose:2-PII(D28)	Dose:1-ESFU(D180)
Group		**Protocol**	**Protocol**	**Protocol**	**Protocol**
		from 3 to 17 year	from 25 to 42 days	from 25 to 42 days	from 166 to 201 days
QIV1	N	350	336	320	330
	n	0	5	6	2
	%	0.0	1.5	1.9	0.6
	range	3 to 8	25 to 58	19 to 53	166 to 209
TIV-VB	N	339	333	320	316
	n	0	6	4	1
	%	0.0	1.8	1.3	0.3
	range	3 to 8	25 to 56	14 to 50	162 to 200
TIV-YB	N	337	330	317	320
	n	0	5	6	2
	%	0.0	1.5	1.9	0.6
	range	3 to 9	25 to 56	23 to 56	165 to 202

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Supplement 5 Deviations from specifications for age and intervals between study visits for primed subjects (6 to 35 months old) (TVC)

		Age	Dose:1-PI(D28)	Dose:1-ESFU(D180)
Group		**Protocol**	**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days	from 166 to 201 days
QIV2	N	59	55	57
	n	0	0	0
	%	0.0	0.0	0.0
	range	13 to 35	25 to 40	166 to 199

QIV2 = Flu Q-QIV (6 - 35 months)
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Supplement 6 Deviations from specifications for age and intervals between study visits for unprimed subjects (6 to 35 months old) (TVC)

		Age	Dose:1-PI(D28)	Dose:2-PII(D28)	Dose:1-ESFU(D180)
Group		**Protocol**	**Protocol**	**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days	from 25 to 42 days	from 166 to 201 days
QIV2	N	242	235	224	218
	n	0	4	10	5
	%	0.0	1.7	4.5	2.3
	range	6 to 35	25 to 51	14 to 112	165 to 215

TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Supplement 7 History of Influenza Vaccination in the previous three seasons (TVC)

		QIV1 N = 932		TIV-VB N = 929		TIV-YB N = 932		QIV2 N = 301		Total N = 3094	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one season	Yes	581	62.3	586	63.1	595	63.8	157	52.2	1919	62.0
	No	351	37.7	343	36.9	337	36.2	144	47.8	1175	38.0
Season 2007-2008	Yes	245	26.3	234	25.2	251	26.9	1	0.3	731	23.6
Season 2008-2009	Yes	309	33.2	322	34.7	317	34.0	48	15.9	996	32.2
Season 2009-2010	Yes	508	54.5	525	56.5	530	56.9	150	49.8	1713	55.4

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
N = Total number of subjects
n = number of subjects with influenza vaccination during the specified season
% = n / Number of subjects with available results x 100

Supplement 8 Adjusted GMT ratios of HI antibody post last vaccination between the groups TIV-VB+ TIV-YB and QIV1 for the A/California/7/2009 (H1N1) strain (Total vaccinated cohort)

				Adjusted GMT ratio (TIV-VB+TIV-YB / QIV1)		
TIV-VB+TIV-YB		**QIV1**			**95% CI**	
N	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
1787	419.0	887	366.7	1.14	1.05	1.24

TIV-VB+TIV-YB = Pooled TIV groups
QIV1 = Flu Q-QIV (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Supplement 9 Adjusted GMT ratios of HI antibody post last vaccination between the groups TIV-VB+ TIV-YB and QIV1 for the A/Victoria/210/2009 (H3N2) strain (Total vaccinated cohort)

				Adjusted GMT ratio (TIV-VB+TIV-YB / QIV1)		
TIV-VB+TIV-YB		**QIV1**			**95% CI**	
N	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
1785	143.8	887	146.1	0.98	0.91	1.06

TIV-VB+TIV-YB = Pooled TIV groups
QIV1 = Flu Q-QIV (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Supplement 10 Adjusted GMT ratios of HI antibody post last vaccination between the groups TIV-VB and QIV1 for the B/Brisbane/60/2008 (Victoria) strain (Total vaccinated cohort)

				Adjusted GMT ratio (TIV-VB / QIV1)		
TIV-VB		QIV1			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
890	243.0	887	252.3	0.96	0.87	1.07

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Supplement 11 Adjusted GMT ratios of HI antibody post last vaccination between the groups TIV-YB and QIV1 for the B/Florida/4/2006 (Yamagata) strain (Total vaccinated cohort)

				Adjusted GMT ratio (TIV-YB / QIV1)		
TIV-YB		QIV1			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
897	559.1	887	525.2	1.06	0.98	1.15

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Supplement 12 Difference in Seroconversion rate (SCR) of HI antibody post last vaccination between the groups TIV-VB+ TIV-YB and QIV1 for the A/California/7/2009 (H1N1) strain (Total vaccinated cohort)

								Difference in vaccine response rate (TIV-VB+TIV-YB minus QIV1)		
		QIV1			TIV-VB+TIV-YB				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
A/California/7/2009 (H1N1) (1/DIL)	Total	887	749	84.4	1787	1540	86.2	1.74	-1.06	4.69

TIV-VB+TIV-YB = Pooled TIV groups
QIV1 = Flu Q-QIV (3 - 17 years)
S- = seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as :
For initially seronegative subjects : post-vaccination antibody titer ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titer at POST ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Supplement 13 Difference in Seroconversion rate (SCR) of HI antibody post last vaccination between the groups TIV-VB+ TIV-YB and QIV1 for the A/Victoria/210/2009 (H3N2) strain (Total vaccinated cohort)

								Difference in vaccine response rate (TIV-VB+TIV-YB minus QIV1)		
		QIV1			TIV-VB+TIV-YB				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
A/Victoria/210/2009 (H3N2) (1/DIL)	Total	887	622	70.1	1785	1222	68.5	-1.66	-5.32	2.08

TIV-VB+TIV-YB = Pooled TIV groups
QIV1 = Flu Q-QIV (3 - 17 years)
S- = seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as :
For initially seronegative subjects : post-vaccination antibody titer ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titer at POST ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Supplement 14 Difference in Seroconversion rate (SCR) of HI antibody post last vaccination between the groups TIV-VB and QIV1 for the B/Brisbane/60/2008 (Victoria) strain (Total vaccinated cohort)

								Difference in vaccine response rate (TIV-VB minus QIV1)		
		QIV1			TIV-VB				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
B/Brisbane/60/2008 (Victoria) (1/DIL)	Total	887	663	74.7	890	640	71.9	-2.84	-6.94	1.28

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
S- = seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as :
For initially seronegative subjects : post-vaccination antibody titer ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titer at POST ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Supplement 15 Difference in Seroconversion rate (SCR) of HI antibody post last vaccination between the groups TIV-YB and QIV1 for the B/Florida/4/2006 Yamagata strain (Total vaccinated cohort)

								Difference in vaccine response rate (TIV-YB minus QIV1)		
		QIV1			TIV-YB				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
B/Florida/4/2006 (Yamagata) (1/DIL)	Total	887	669	75.4	897	660	73.6	-1.84	-5.89	2.20

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
S- = seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as :
For initially seronegative subjects : post-vaccination antibody titer ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titer at POST ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Supplement 16 Adjusted GMT ratios of HI antibody post last vaccination between the groups QIV1 and TIV-VB for the Flu B/Florida/4/2006 (Yamagata) strain (Total vaccinated cohort)

				Adjusted GMT ratio (QIV1 / TIV-VB)		
QIV1		TIV-VB			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
887	512.5	890	195.9	2.62	2.41	2.84

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Supplement 17 Adjusted GMT ratios of HI antibody post last vaccination between the groups QIV1 and TIV-YB for the B/Brisbane/60/2008 (Victoria) strain (Total vaccinated cohort)

				Adjusted GMT ratio (QIV1 / TIV-YB)		
QIV1		TIV-YB			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
887	253.6	895	66.6	3.81	3.46	4.19

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Supplement 18 Superiority of QIV1 versus TIV-VB in terms of seroconversion rate (difference in seroconversion rate) at day 28 for the B/Florida/4/2006 (Yamagata) strain (Total vaccinated cohort)

								Difference in vaccine response rate (QIV1 minus TIV-VB)		
		QIV1			TIV-VB				95% CI	
Antibody	**Pre-vaccination status**	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
B/Florida/4/2006 (Yamagata) (1/DIL)	Total	887	669	75.4	890	372	41.8	33.63	29.26	37.86

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
S- = seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as :
For initially seronegative subjects : post-vaccination antibody titer ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titer at POST ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Supplement 19 Superiority of QIV1 versus TIV-YB in terms of seroconversion rate (difference in seroconversion rate) at day 28 for the the B/Brisbane/60/2008 (Victoria) strain (Total vaccinated cohort)

								Difference in vaccine response rate (QIV1 minus TIV-YB)		
		QIV1			TIV-YB				95% CI	
Antibody	**Pre-vaccination status**	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
B/Brisbane/60/2008 (Victoria) (1/DIL)	Total	887	663	74.7	895	266	29.7	45.03	40.79	49.07

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
S- = seronegative subjects (antibody titer < 10 1/DIL) prior to vaccination
S+ = seropositive subjects (antibody titer ≥ 10 1/DIL) prior to vaccination
Vaccine response defined as :
For initially seronegative subjects : post-vaccination antibody titer ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titer at POST ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Supplement 20 Seropositivity rates and GMTs for HI antibody titers by age strata (3-8y/9-17y) (ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/ 2009 (H1N1)	QIV1	3-8y	PRE	423	273	64.5	59.8	69.1	24.7	21.6	28.3
			POST	425	421	99.1	97.6	99.7	310.5	274.9	350.6
		9-17y	PRE	453	356	78.6	74.5	82.3	34.6	30.6	39.2
			POST	453	450	99.3	98.1	99.9	419.5	379.8	463.4
	TIV-VB	3-8y	PRE	423	278	65.7	61.0	70.2	26.9	23.5	30.9
			POST	424	421	99.3	97.9	99.9	382.7	339.4	431.6
		9-17y	PRE	447	363	81.2	77.3	84.7	38.2	33.8	43.1
			POST	447	444	99.3	98.1	99.9	478.2	431.4	530.0
	TIV-YB	3-8y	PRE	424	283	66.7	62.0	71.2	24.5	21.5	27.8
			POST	424	422	99.5	98.3	99.9	356.2	316.5	400.8
		9-17y	PRE	453	356	78.6	74.5	82.3	34.2	30.3	38.6
			POST	454	454	100	99.2	100	490.3	443.7	541.7
A/Victoria/210/ 2009 (H3N2)	QIV1	3-8y	PRE	423	269	63.6	58.8	68.2	19.7	17.4	22.4
			POST	425	420	98.8	97.3	99.6	138.2	123.7	154.5
		9-17y	PRE	453	297	65.6	61.0	69.9	16.7	15.0	18.7
			POST	453	452	99.8	98.8	100	149.1	137.3	162.0
	TIV-VB	3-8y	PRE	423	270	63.8	59.0	68.4	21.2	18.6	24.2
			POST	424	418	98.6	96.9	99.5	144.4	130.6	159.7
		9-17y	PRE	447	308	68.9	64.4	73.2	17.0	15.3	19.0
			POST	447	444	99.3	98.1	99.9	135.2	123.5	148.0
	TIV-YB	3-8y	PRE	423	266	62.9	58.1	67.5	20.2	17.8	23.0
			POST	424	418	98.6	96.9	99.5	147.9	133.3	164.1
		9-17y	PRE	453	302	66.7	62.1	71.0	18.6	16.6	20.9
			POST	454	453	99.8	98.8	100	153.9	140.7	168.4
B/Brisbane/60/ 2008 (Victoria)	QIV1	3-8y	PRE	423	230	54.4	49.5	59.2	18.3	15.8	21.1
			POST	425	419	98.6	97.0	99.5	194.4	171.3	220.7
		9-17y	PRE	453	357	78.8	74.8	82.5	32.9	29.0	37.4
			POST	453	452	99.8	98.8	100	317.8	287.1	351.8
	TIV-VB	3-8y	PRE	423	246	58.2	53.3	62.9	20.2	17.6	23.3
			POST	424	417	98.3	96.6	99.3	197.4	175.9	221.6
		9-17y	PRE	447	351	78.5	74.4	82.2	32.5	28.7	36.8
			POST	447	445	99.6	98.4	99.9	301.7	272.2	334.3
	TIV-YB	3-8y	PRE	424	238	56.1	51.3	60.9	18.4	16.0	21.1
			POST	423	360	85.1	81.4	88.4	52.6	45.2	61.2
		9-17y	PRE	453	373	82.3	78.5	85.7	35.4	31.3	40.1
			POST	454	432	95.2	92.8	96.9	86.6	77.4	96.9
B/Florida/4/2006 (Yamagata)	QIV1	3-8y	PRE	423	289	68.3	63.7	72.7	27.4	23.8	31.7
			POST	425	424	99.8	98.7	100	363.4	327.8	402.9
		9-17y	PRE	453	426	94.0	91.4	96.0	116.2	102.2	132.1
			POST	453	453	100	99.2	100	707.5	648.7	771.5
	TIV-VB	3-8y	PRE	423	300	70.9	66.3	75.2	29.5	25.6	34.0
			POST	424	410	96.7	94.5	98.2	103.2	91.7	116.1
		9-17y	PRE	447	417	93.3	90.6	95.4	111.6	98.3	126.8
			POST	447	446	99.8	98.8	100	363.7	330.4	400.3
	TIV-YB	3-8y	PRE	424	286	67.5	62.8	71.9	29.5	25.5	34.1
			POST	424	423	99.8	98.7	100	416.7	374.5	463.7
		9-17y	PRE	453	439	96.9	94.9	98.3	139.6	124.6	156.4
			POST	454	454	100	99.2	100	787.1	731.3	847.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 21 Seroconversion rate (SCR) for HI antibody titers post last vaccination by age strata (3-8y/9-17y) (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	3-8y	423	374	88.4	85.0	91.3
		9-17y	453	365	80.6	76.6	84.1
	TIV-VB	3-8y	423	390	92.2	89.2	94.6
		9-17y	447	365	81.7	77.8	85.1
	TIV-YB	3-8y	424	380	89.6	86.3	92.4
		9-17y	453	370	81.7	77.8	85.1
A/Victoria/210/2009 (H3N2)	QIV1	3-8y	423	291	68.8	64.1	73.2
		9-17y	453	323	71.3	66.9	75.4
	TIV-VB	3-8y	423	282	66.7	62.0	71.1
		9-17y	447	308	68.9	64.4	73.2
	TIV-YB	3-8y	423	296	70.0	65.4	74.3
		9-17y	453	314	69.3	64.8	73.5
B/Brisbane/60/2008 (Victoria)	QIV1	3-8y	423	329	77.8	73.5	81.7
		9-17y	453	324	71.5	67.1	75.6
	TIV-VB	3-8y	423	326	77.1	72.8	81.0
		9-17y	447	296	66.2	61.6	70.6
	TIV-YB	3-8y	423	133	31.4	27.0	36.1
		9-17y	453	129	28.5	24.4	32.9
B/Florida/4/2006 (Yamagata)	QIV1	3-8y	423	366	86.5	82.9	89.6
		9-17y	453	293	64.7	60.1	69.1
	TIV-VB	3-8y	423	181	42.8	38.0	47.7
		9-17y	447	178	39.8	35.3	44.5
	TIV-YB	3-8y	424	372	87.7	84.2	90.7
		9-17y	453	272	60.0	55.4	64.6

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 22 Seroprotection rates for HI antibody titers by age strata (3-8y/9-17y) (ATP cohort for immunogenicity)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	3-8y	PRE	423	209	49.4	44.5	54.3
			POST	425	405	95.3	92.8	97.1
		9-17y	PRE	453	271	59.8	55.1	64.4
			POST	453	445	98.2	96.6	99.2
	TIV-VB	3-8y	PRE	423	218	51.5	46.7	56.4
			POST	424	412	97.2	95.1	98.5
		9-17y	PRE	447	278	62.2	57.5	66.7
			POST	447	436	97.5	95.6	98.8
	TIV-YB	3-8y	PRE	424	207	48.8	44.0	53.7
			POST	424	405	95.5	93.1	97.3
		9-17y	PRE	453	270	59.6	54.9	64.2
			POST	454	443	97.6	95.7	98.8
A/Victoria/210/2009 (H3N2)	QIV1	3-8y	PRE	423	161	38.1	33.4	42.9
			POST	425	379	89.2	85.8	92.0
		9-17y	PRE	453	134	29.6	25.4	34.0
			POST	453	437	96.5	94.3	98.0
	TIV-VB	3-8y	PRE	423	174	41.1	36.4	46.0
			POST	424	390	92.0	89.0	94.4
		9-17y	PRE	447	127	28.4	24.3	32.8
			POST	447	418	93.5	90.8	95.6
	TIV-YB	3-8y	PRE	423	168	39.7	35.0	44.6
			POST	424	389	91.7	88.7	94.2
		9-17y	PRE	453	156	34.4	30.1	39.0
			POST	454	430	94.7	92.2	96.6
B/Brisbane/60/2008 (Victoria)	QIV1	3-8y	PRE	423	144	34.0	29.5	38.8
			POST	425	398	93.6	90.9	95.8
		9-17y	PRE	453	244	53.9	49.1	58.5
			POST	453	440	97.1	95.1	98.5
	TIV-VB	3-8y	PRE	423	163	38.5	33.9	43.4
			POST	424	406	95.8	93.4	97.5
		9-17y	PRE	447	241	53.9	49.2	58.6
			POST	447	433	96.9	94.8	98.3
	TIV-YB	3-8y	PRE	424	150	35.4	30.8	40.1
			POST	423	271	64.1	59.3	68.6
		9-17y	PRE	453	250	55.2	50.5	59.8
			POST	454	372	81.9	78.1	85.4
B/Florida/4/2006 (Yamagata)	QIV1	3-8y	PRE	423	205	48.5	43.6	53.3
			POST	425	419	98.6	97.0	99.5
		9-17y	PRE	453	373	82.3	78.5	85.7
			POST	453	450	99.3	98.1	99.9
	TIV-VB	3-8y	PRE	423	209	49.4	44.5	54.3
			POST	424	361	85.1	81.4	88.4
		9-17y	PRE	447	374	83.7	79.9	87.0
			POST	447	444	99.3	98.1	99.9
	TIV-YB	3-8y	PRE	424	220	51.9	47.0	56.7
			POST	424	420	99.1	97.6	99.7
		9-17y	PRE	453	402	88.7	85.5	91.5
			POST	454	453	99.8	98.8	100

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 23 Seroconversion Factor (SCF) for HI antibody titers post vaccination by age strata (3-8y/9-17y) (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1) (1/DIL)	QIV1	3-8y	423	12.50	11.31	13.82
		9-17y	453	12.12	10.67	13.77
	TIV-VB	3-8y	423	14.20	12.83	15.71
		9-17y	447	12.52	11.07	14.17
	TIV-YB	3-8y	424	14.56	13.20	16.05
		9-17y	453	14.29	12.52	16.31
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	3-8y	423	7.02	6.30	7.84
		9-17y	453	8.91	7.85	10.11
	TIV-VB	3-8y	423	6.82	6.09	7.64
		9-17y	447	7.94	7.02	8.97
	TIV-YB	3-8y	423	7.29	6.51	8.16
		9-17y	453	8.27	7.32	9.34
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	3-8y	423	10.64	9.41	12.02
		9-17y	453	9.65	8.42	11.07
	TIV-VB	3-8y	423	9.75	8.61	11.04
		9-17y	447	9.28	8.04	10.71
	TIV-YB	3-8y	423	2.85	2.58	3.16
		9-17y	453	2.44	2.25	2.65
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	3-8y	423	13.23	11.74	14.90
		9-17y	453	6.09	5.42	6.84
	TIV-VB	3-8y	423	3.49	3.18	3.84
		9-17y	447	3.26	2.93	3.62
	TIV-YB	3-8y	424	14.11	12.57	15.84
		9-17y	453	5.63	5.02	6.33

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 24 Seropositivity rates and GMTs for HI antibody titers by previous influenza vaccination status (ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	307	177	57.7	51.9	63.2	22.7	19.2	26.7
			POST	309	307	99.4	97.7	99.9	319.7	277.5	368.2
		prim	PRE	569	452	79.4	75.9	82.7	33.8	30.3	37.7
			POST	569	564	99.1	98.0	99.7	388.4	353.7	426.5
	TIV-VB	Unprm	PRE	308	194	63.0	57.3	68.4	26.4	22.5	31.1
			POST	308	306	99.4	97.7	99.9	399.8	347.9	459.5
		prim	PRE	562	447	79.5	76.0	82.8	35.9	32.2	40.1
			POST	563	559	99.3	98.2	99.8	445.9	405.2	490.8
	TIV-YB	Unprm	PRE	306	195	63.7	58.1	69.1	24.6	21.1	28.7
			POST	306	304	99.3	97.7	99.9	387.0	337.1	444.4
		prim	PRE	571	444	77.8	74.1	81.1	31.8	28.6	35.4
			POST	572	572	100	99.4	100	439.0	400.0	481.9
	QIV2	Unprm	PRE	204	73	35.8	29.2	42.8	14.8	11.9	18.4
			POST	204	200	98.0	95.1	99.5	167.8	135.7	207.5
		prim	PRE	55	43	78.2	65.0	88.2	27.1	19.0	38.5
			POST	55	55	100	93.5	100	391.5	275.2	556.8
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	307	195	63.5	57.9	68.9	19.7	17.0	22.9
			POST	309	307	99.4	97.7	99.9	146.6	129.6	165.8
		prim	PRE	569	371	65.2	61.1	69.1	17.3	15.7	19.1
			POST	569	565	99.3	98.2	99.8	142.2	131.0	154.4
	TIV-VB	Unprm	PRE	308	201	65.3	59.7	70.6	21.0	18.1	24.4
			POST	308	307	99.7	98.2	100	155.4	139.2	173.4
		prim	PRE	562	377	67.1	63.0	71.0	17.9	16.1	19.9
			POST	563	555	98.6	97.2	99.4	131.7	121.0	143.4
	TIV-YB	Unprm	PRE	305	193	63.3	57.6	68.7	20.0	17.2	23.2
			POST	306	304	99.3	97.7	99.9	165.0	146.9	185.3
		prim	PRE	571	375	65.7	61.6	69.6	19.1	17.1	21.2
			POST	572	567	99.1	98.0	99.7	144.0	132.4	156.6
	QIV2	Unprm	PRE	204	12	5.9	3.1	10.0	5.6	5.2	6.0
			POST	204	198	97.1	93.7	98.9	59.7	51.3	69.5
		prim	PRE	55	6	10.9	4.1	22.2	5.6	5.1	6.2
			POST	55	54	98.2	90.3	100	67.9	52.0	88.7
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	307	158	51.5	45.7	57.2	17.7	15.0	20.9
			POST	309	308	99.7	98.2	100	218.3	190.2	250.5
		prim	PRE	569	429	75.4	71.6	78.9	29.7	26.5	33.4
			POST	569	563	98.9	97.7	99.6	270.0	243.8	299.0
	TIV-VB	Unprm	PRE	308	174	56.5	50.8	62.1	20.0	17.0	23.7
			POST	308	306	99.4	97.7	99.9	227.8	199.7	260.0
		prim	PRE	562	423	75.3	71.5	78.8	29.7	26.5	33.2
			POST	563	556	98.8	97.5	99.5	255.6	231.9	281.8
	TIV-YB	Unprm	PRE	306	162	52.9	47.2	58.6	18.2	15.4	21.5
			POST	305	250	82.0	77.2	86.1	51.6	42.8	62.3
		prim	PRE	571	449	78.6	75.0	81.9	31.1	27.8	34.8
			POST	572	542	94.8	92.6	96.4	78.9	71.2	87.5
	QIV2	Unprm	PRE	204	44	21.6	16.1	27.9	7.5	6.5	8.6
			POST	204	200	98.0	95.1	99.5	115.9	97.8	137.3
		prim	PRE	55	32	58.2	44.1	71.3	15.1	10.2	22.6
			POST	55	55	100	93.5	100	180.3	129.6	250.8

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	307	196	63.8	58.2	69.2	26.0	21.9	30.9
			POST	309	309	100	98.8	100	378.2	338.5	422.6
		prim	PRE	569	519	91.2	88.6	93.4	89.1	78.8	100.7
			POST	569	568	99.8	99.0	100	604.4	553.6	659.8
	TIV-VB	Unprm	PRE	308	208	67.5	62.0	72.7	28.2	23.7	33.5
			POST	308	296	96.1	93.3	98.0	98.0	84.9	113.2
		prim	PRE	562	509	90.6	87.8	92.9	87.1	77.2	98.3
			POST	563	560	99.5	98.5	99.9	288.5	262.6	317.1
	TIV-YB	Unprm	PRE	306	196	64.1	58.4	69.4	27.9	23.4	33.2
			POST	306	306	100	98.8	100	447.5	397.4	503.9
		prim	PRE	571	529	92.6	90.2	94.6	104.5	93.2	117.1
			POST	572	571	99.8	99.0	100	664.5	613.7	719.6
	QIV2	Unprm	PRE	204	36	17.6	12.7	23.6	6.3	5.8	6.9
			POST	204	204	100	98.2	100	189.9	169.4	213.0
		prim	PRE	55	33	60.0	45.9	73.0	16.3	11.7	22.8
			POST	55	54	98.2	90.3	100	203.3	146.1	282.8

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 25 Seroconversion rate (SCR) for HI antibody titers post last vaccination by previous influenza vaccination status (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	307	278	90.6	86.7	93.6
		prim	569	461	81.0	77.6	84.2
	TIV-VB	Unprm	308	288	93.5	90.1	96.0
		prim	562	467	83.1	79.7	86.1
	TIV-YB	Unprm	306	281	91.8	88.2	94.6
		prim	571	469	82.1	78.7	85.2
	QIV2	Unprm	204	169	82.8	77.0	87.7
		prim	55	51	92.7	82.4	98.0
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	307	217	70.7	65.2	75.7
		prim	569	397	69.8	65.8	73.5
	TIV-VB	Unprm	308	220	71.4	66.0	76.4
		prim	562	370	65.8	61.8	69.8
	TIV-YB	Unprm	305	230	75.4	70.2	80.1
		prim	571	380	66.5	62.5	70.4
	QIV2	Unprm	204	148	72.5	65.9	78.5
		prim	55	41	74.5	61.0	85.3
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	307	251	81.8	77.0	85.9
		prim	569	402	70.7	66.7	74.4
	TIV-VB	Unprm	308	250	81.2	76.3	85.4
		prim	562	372	66.2	62.1	70.1
	TIV-YB	Unprm	305	94	30.8	25.7	36.3
		prim	571	168	29.4	25.7	33.3
	QIV2	Unprm	204	172	84.3	78.6	89.0
		prim	55	47	85.5	73.3	93.5
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	307	269	87.6	83.4	91.1
		prim	569	390	68.5	64.5	72.3
	TIV-VB	Unprm	308	130	42.2	36.6	47.9
		prim	562	229	40.7	36.7	44.9
	TIV-YB	Unprm	306	273	89.2	85.2	92.5
		prim	571	371	65.0	60.9	68.9
	QIV2	Unprm	204	197	96.6	93.1	98.6
		prim	55	46	83.6	71.2	92.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 26 Seroprotection rates for HI antibody titers by previous influenza vaccination status (ATP cohort for immunogenicity)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	307	148	48.2	42.5	54.0
			POST	309	296	95.8	92.9	97.7
		prim	PRE	569	332	58.3	54.2	62.4
			POST	569	554	97.4	95.7	98.5
	TIV-VB	Unprm	PRE	308	164	53.2	47.5	58.9
			POST	308	299	97.1	94.5	98.7
		prim	PRE	562	332	59.1	54.9	63.2
			POST	563	549	97.5	95.9	98.6
	TIV-YB	Unprm	PRE	306	159	52.0	46.2	57.7
			POST	306	294	96.1	93.3	98.0
		prim	PRE	571	318	55.7	51.5	59.8
			POST	572	554	96.9	95.1	98.1
	QIV2	Unprm	PRE	204	63	30.9	24.6	37.7
			POST	204	179	87.7	82.4	91.9
		prim	PRE	55	24	43.6	30.3	57.7
			POST	55	53	96.4	87.5	99.6
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	307	115	37.5	32.0	43.1
			POST	309	281	90.9	87.2	93.9
		prim	PRE	569	180	31.6	27.8	35.6
			POST	569	535	94.0	91.7	95.8
	TIV-VB	Unprm	PRE	308	127	41.2	35.7	47.0
			POST	308	289	93.8	90.5	96.2
		prim	PRE	562	174	31.0	27.2	35.0
			POST	563	519	92.2	89.7	94.3
	TIV-YB	Unprm	PRE	305	122	40.0	34.5	45.7
			POST	306	287	93.8	90.5	96.2
		prim	PRE	571	202	35.4	31.5	39.5
			POST	572	532	93.0	90.6	95.0
	QIV2	Unprm	PRE	204	7	3.4	1.4	6.9
			POST	204	152	74.5	68.0	80.3
		prim	PRE	55	0	0.0	0.0	6.5
			POST	55	41	74.5	61.0	85.3
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	307	105	34.2	28.9	39.8
			POST	309	296	95.8	92.9	97.7
		prim	PRE	569	283	49.7	45.6	53.9
			POST	569	542	95.3	93.2	96.8
	TIV-VB	Unprm	PRE	308	119	38.6	33.2	44.3
			POST	308	301	97.7	95.4	99.1
		prim	PRE	562	285	50.7	46.5	54.9
			POST	563	538	95.6	93.5	97.1
	TIV-YB	Unprm	PRE	306	109	35.6	30.3	41.3
			POST	305	188	61.6	55.9	67.1
		prim	PRE	571	291	51.0	46.8	55.1
			POST	572	455	79.5	76.0	82.8
	QIV2	Unprm	PRE	204	15	7.4	4.2	11.8
			POST	204	177	86.8	81.3	91.1
		prim	PRE	55	13	23.6	13.2	37.0
			POST	55	51	92.7	82.4	98.0

					SPR			
							95% CI	
Strain	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	307	147	47.9	42.2	53.6
			POST	309	308	99.7	98.2	100
		prim	PRE	569	431	75.7	72.0	79.2
			POST	569	561	98.6	97.2	99.4
	TIV-VB	Unprm	PRE	308	147	47.7	42.0	53.5
			POST	308	256	83.1	78.5	87.1
		prim	PRE	562	436	77.6	73.9	81.0
			POST	563	549	97.5	95.9	98.6
	TIV-YB	Unprm	PRE	306	153	50.0	44.3	55.7
			POST	306	304	99.3	97.7	99.9
		prim	PRE	571	469	82.1	78.7	85.2
			POST	572	569	99.5	98.5	99.9
	QIV2	Unprm	PRE	204	7	3.4	1.4	6.9
			POST	204	200	98.0	95.1	99.5
		prim	PRE	55	15	27.3	16.1	41.0
			POST	55	50	90.9	80.0	97.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 27 Seroconversion Factor (SCF) for HI antibody titers post last vaccination by previous influenza vaccination status (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Strain	Group	Sub-group	N	Value	LL	UL
A/California/7/2009 (H1N1) (1/DIL)	QIV1	Unprm	307	13.99	12.50	15.66
		prim	569	11.48	10.29	12.81
	TIV-VB	Unprm	308	15.12	13.50	16.94
		prim	562	12.41	11.15	13.82
	TIV-YB	Unprm	306	15.71	14.08	17.54
		prim	571	13.77	12.30	15.41
	QIV2	Unprm	204	11.35	9.85	13.08
		prim	55	14.47	10.74	19.51
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	Unprm	307	7.46	6.55	8.49
		prim	569	8.22	7.36	9.17
	TIV-VB	Unprm	308	7.39	6.51	8.38
		prim	562	7.36	6.60	8.22
	TIV-YB	Unprm	305	8.21	7.21	9.33
		prim	571	7.56	6.79	8.42
	QIV2	Unprm	204	10.66	9.22	12.33
		prim	55	12.06	9.29	15.66
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	Unprm	307	12.35	10.71	14.24
		prim	569	9.09	8.07	10.22
	TIV-VB	Unprm	308	11.37	9.85	13.13
		prim	562	8.62	7.61	9.75
	TIV-YB	Unprm	305	2.83	2.50	3.20
		prim	571	2.53	2.35	2.73
	QIV2	Unprm	204	15.44	13.35	17.87
		prim	55	11.90	8.98	15.77
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	Unprm	307	14.51	12.60	16.71
		prim	569	6.79	6.12	7.53
	TIV-VB	Unprm	308	3.48	3.11	3.89
		prim	562	3.31	3.02	3.63
	TIV-YB	Unprm	306	16.06	13.96	18.47
		prim	571	6.35	5.74	7.04
	QIV2	Unprm	204	30.06	26.38	34.24
		prim	55	12.44	9.42	16.44

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 28 **Seropositivity rates and GMTs for HI antibody titers by previous influenza vaccination status for subjects aged between 3 to 8 years old (ATP cohort for immunogenicity)**

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	307	177	57.7	51.9	63.2	22.7	19.2	26.7
			POST	309	307	99.4	97.7	99.9	319.7	277.5	368.2
		prim	PRE	116	96	82.8	74.6	89.1	30.9	24.5	39.1
			POST	116	114	98.3	93.9	99.8	287.3	225.8	365.7
	TIV-VB	Unprm	PRE	308	194	63.0	57.3	68.4	26.4	22.5	31.1
			POST	308	306	99.4	97.7	99.9	399.8	347.9	459.5
		prim	PRE	115	84	73.0	64.0	80.9	28.4	22.0	36.5
			POST	116	115	99.1	95.3	100	340.7	268.1	433.0
	TIV-YB	Unprm	PRE	306	195	63.7	58.1	69.1	24.6	21.1	28.7
			POST	306	304	99.3	97.7	99.9	387.0	337.1	444.4
		prim	PRE	118	88	74.6	65.7	82.1	24.0	19.1	30.3
			POST	118	118	100	96.9	100	287.1	229.2	359.6
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	307	195	63.5	57.9	68.9	19.7	17.0	22.9
			POST	309	307	99.4	97.7	99.9	146.6	129.6	165.8
		prim	PRE	116	74	63.8	54.4	72.5	19.8	15.5	25.2
			POST	116	113	97.4	92.6	99.5	118.3	93.0	150.4
	TIV-VB	Unprm	PRE	308	201	65.3	59.7	70.6	21.0	18.1	24.4
			POST	308	307	99.7	98.2	100	155.4	139.2	173.4
		prim	PRE	115	69	60.0	50.4	69.0	21.7	16.3	28.9
			POST	116	111	95.7	90.2	98.6	119.0	95.2	148.8
	TIV-YB	Unprm	PRE	305	193	63.3	57.6	68.7	20.0	17.2	23.2
			POST	306	304	99.3	97.7	99.9	165.0	146.9	185.3
		prim	PRE	118	73	61.9	52.5	70.6	20.8	15.9	27.2
			POST	118	114	96.6	91.5	99.1	111.4	89.9	138.1
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	307	158	51.5	45.7	57.2	17.7	15.0	20.9
			POST	309	308	99.7	98.2	100	218.3	190.2	250.5
		prim	PRE	116	72	62.1	52.6	70.9	19.9	15.1	26.3
			POST	116	111	95.7	90.2	98.6	142.8	108.0	188.9
	TIV-VB	Unprm	PRE	308	174	56.5	50.8	62.1	20.0	17.0	23.7
			POST	308	306	99.4	97.7	99.9	227.8	199.7	260.0
		prim	PRE	115	72	62.6	53.1	71.5	20.7	15.9	27.1
			POST	116	111	95.7	90.2	98.6	135.0	107.7	169.1
	TIV-YB	Unprm	PRE	306	162	52.9	47.2	58.6	18.2	15.4	21.5
			POST	305	250	82.0	77.2	86.1	51.6	42.8	62.3
		prim	PRE	118	76	64.4	55.1	73.0	18.9	14.7	24.3
			POST	118	110	93.2	87.1	97.0	55.2	43.3	70.5
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	307	196	63.8	58.2	69.2	26.0	21.9	30.9
			POST	309	309	100	98.8	100	378.2	338.5	422.6
		prim	PRE	116	93	80.2	71.7	87.0	31.6	24.4	40.8
			POST	116	115	99.1	95.3	100	326.8	257.7	414.5
	TIV-VB	Unprm	PRE	308	208	67.5	62.0	72.7	28.2	23.7	33.5
			POST	308	296	96.1	93.3	98.0	98.0	84.9	113.2
		prim	PRE	115	92	80.0	71.5	86.9	33.3	25.8	42.8
			POST	116	114	98.3	93.9	99.8	118.3	96.6	144.8

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
	TIV-YB	Unprm	PRE	306	196	64.1	58.4	69.4	27.9	23.4	33.2
			POST	306	306	100	98.8	100	447.5	397.4	503.9
		prim	PRE	118	90	76.3	67.6	83.6	34.3	26.5	44.4
			POST	118	117	99.2	95.4	100	346.4	275.4	435.8

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 29 Seroconversion rate (SCR) for HI antibody titers post last vaccination by previous influenza vaccination status for subjects aged between 3 to 8 years old (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	307	278	90.6	86.7	93.6
		prim	116	96	82.8	74.6	89.1
	TIV-VB	Unprm	308	288	93.5	90.1	96.0
		prim	115	102	88.7	81.4	93.8
	TIV-YB	Unprm	306	281	91.8	88.2	94.6
		prim	118	99	83.9	76.0	90.0
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	307	217	70.7	65.2	75.7
		prim	116	74	63.8	54.4	72.5
	TIV-VB	Unprm	308	220	71.4	66.0	76.4
		prim	115	62	53.9	44.4	63.2
	TIV-YB	Unprm	305	230	75.4	70.2	80.1
		prim	118	66	55.9	46.5	65.1
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	307	251	81.8	77.0	85.9
		prim	116	78	67.2	57.9	75.7
	TIV-VB	Unprm	308	250	81.2	76.3	85.4
		prim	115	76	66.1	56.7	74.7
	TIV-YB	Unprm	305	94	30.8	25.7	36.3
		prim	118	39	33.1	24.7	42.3
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	307	269	87.6	83.4	91.1
		prim	116	97	83.6	75.6	89.8
	TIV-VB	Unprm	308	130	42.2	36.6	47.9
		prim	115	51	44.3	35.1	53.9
	TIV-YB	Unprm	306	273	89.2	85.2	92.5
		prim	118	99	83.9	76.0	90.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 30 Seroprotection rates for HI antibody titers by previous influenza vaccination status for subjects aged between 3 to 8 years old (ATP cohort for immunogenicity)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	307	148	48.2	42.5	54.0
			POST	309	296	95.8	92.9	97.7
		prim	PRE	116	61	52.6	43.1	61.9
			POST	116	109	94.0	88.0	97.5
	TIV-VB	Unprm	PRE	308	164	53.2	47.5	58.9
			POST	308	299	97.1	94.5	98.7
		prim	PRE	115	54	47.0	37.6	56.5
			POST	116	113	97.4	92.6	99.5
	TIV-YB	Unprm	PRE	306	159	52.0	46.2	57.7
			POST	306	294	96.1	93.3	98.0
		prim	PRE	118	48	40.7	31.7	50.1
			POST	118	111	94.1	88.2	97.6
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	307	115	37.5	32.0	43.1
			POST	309	281	90.9	87.2	93.9
		prim	PRE	116	46	39.7	30.7	49.2
			POST	116	98	84.5	76.6	90.5
	TIV-VB	Unprm	PRE	308	127	41.2	35.7	47.0
			POST	308	289	93.8	90.5	96.2
		prim	PRE	115	47	40.9	31.8	50.4
			POST	116	101	87.1	79.6	92.6
	TIV-YB	Unprm	PRE	305	122	40.0	34.5	45.7
			POST	306	287	93.8	90.5	96.2
		prim	PRE	118	46	39.0	30.1	48.4
			POST	118	102	86.4	78.9	92.0
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	307	105	34.2	28.9	39.8
			POST	309	296	95.8	92.9	97.7
		prim	PRE	116	39	33.6	25.1	43.0
			POST	116	102	87.9	80.6	93.2
	TIV-VB	Unprm	PRE	308	119	38.6	33.2	44.3
			POST	308	301	97.7	95.4	99.1
		prim	PRE	115	44	38.3	29.4	47.8
			POST	116	105	90.5	83.7	95.2
	TIV-YB	Unprm	PRE	306	109	35.6	30.3	41.3
			POST	305	188	61.6	55.9	67.1
		prim	PRE	118	41	34.7	26.2	44.1
			POST	118	83	70.3	61.2	78.4
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	307	147	47.9	42.2	53.6
			POST	309	308	99.7	98.2	100
		prim	PRE	116	58	50.0	40.6	59.4
			POST	116	111	95.7	90.2	98.6
	TIV-VB	Unprm	PRE	308	147	47.7	42.0	53.5
			POST	308	256	83.1	78.5	87.1
		prim	PRE	115	62	53.9	44.4	63.2
			POST	116	105	90.5	83.7	95.2
	TIV-YB	Unprm	PRE	306	153	50.0	44.3	55.7
			POST	306	304	99.3	97.7	99.9
		prim	PRE	118	67	56.8	47.3	65.9
			POST	118	116	98.3	94.0	99.8

QIV1 = Flu Q-QIV (3 - 17 years)

TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 31 Seroconversion Factor (SCF) for HI antibody titers post last vaccination by previous influenza vaccination status for subjects aged between 3 to 8 years old (ATP cohort for immunogenicity)

				SCF		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1) (1/DIL)	QIV1	Unprm	307	13.99	12.50	15.66
		prim	116	9.29	7.58	11.38
	TIV-VB	Unprm	308	15.12	13.50	16.94
		prim	115	11.99	9.66	14.87
	TIV-YB	Unprm	306	15.71	14.08	17.54
		prim	118	11.94	9.74	14.63
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	Unprm	307	7.46	6.55	8.49
		prim	116	5.99	4.88	7.35
	TIV-VB	Unprm	308	7.39	6.51	8.38
		prim	115	5.51	4.32	7.01
	TIV-YB	Unprm	305	8.21	7.21	9.33
		prim	118	5.37	4.29	6.72
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	Unprm	307	12.35	10.71	14.24
		prim	116	7.16	5.71	8.99
	TIV-VB	Unprm	308	11.37	9.85	13.13
		prim	115	6.46	5.13	8.14
	TIV-YB	Unprm	305	2.83	2.50	3.20
		prim	118	2.92	2.45	3.48
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	Unprm	307	14.51	12.60	16.71
		prim	116	10.35	8.32	12.89
	TIV-VB	Unprm	308	3.48	3.11	3.89
		prim	115	3.54	2.94	4.26
	TIV-YB	Unprm	306	16.06	13.96	18.47
		prim	118	10.10	8.32	12.25

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 32 Seropositivity rates and GMTs for HI antibody titers by age strata (3-17M/18-35M) (ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)	QIV2	6-17M	PRE	99	18	18.2	11.1	27.2	8.4	6.6	10.8
			POST	99	96	97.0	91.4	99.4	86.1	65.5	113.2
		18-35M	PRE	160	98	61.3	53.2	68.8	25.8	20.1	33.0
			POST	160	159	99.4	96.6	100	339.3	273.5	421.0
A/Victoria/210/2009 (H3N2)	QIV2	6-17M	PRE	99	1	1.0	0.0	5.5	5.0	5.0	5.1
			POST	99	93	93.9	87.3	97.7	40.5	32.8	50.1
		18-35M	PRE	160	17	10.6	6.3	16.5	6.0	5.5	6.6
			POST	160	159	99.4	96.6	100	79.3	67.9	92.7
B/Brisbane/60/2008 (Victoria)	QIV2	6-17M	PRE	99	11	11.1	5.7	19.0	5.8	5.2	6.4
			POST	99	95	96.0	90.0	98.9	72.5	58.0	90.7
		18-35M	PRE	160	65	40.6	32.9	48.7	11.2	9.1	13.9
			POST	160	160	100	97.7	100	180.2	149.9	216.7
B/Florida/4/2006 (Yamagata)	QIV2	6-17M	PRE	99	11	11.1	5.7	19.0	5.6	5.2	6.0
			POST	99	99	100	96.3	100	132.5	112.3	156.2
		18-35M	PRE	160	58	36.3	28.8	44.2	9.4	8.0	11.0
			POST	160	159	99.4	96.6	100	243.0	211.0	280.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 33 Seroconversion rate (SCR) for HI antibody titers post last vaccination by age strata (3-17M/18-35M) (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV2	6-17M	99	76	76.8	67.2	84.7
		18-35M	160	144	90.0	84.3	94.2
A/Victoria/210/2009 (H3N2)	QIV2	6-17M	99	60	60.6	50.3	70.3
		18-35M	160	129	80.6	73.6	86.4
B/Brisbane/60/2008 (Victoria)	QIV2	6-17M	99	79	79.8	70.5	87.2
		18-35M	160	140	87.5	81.4	92.2
B/Florida/4/2006 (Yamagata)	QIV2	6-17M	99	93	93.9	87.3	97.7
		18-35M	160	150	93.8	88.8	97.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 34 Seroprotection rates for HI antibody titers by age strata (3-17M/18-35M) (ATP cohort for immunogenicity)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV2	6-17M	PRE	99	13	13.1	7.2	21.4
			POST	99	79	79.8	70.5	87.2
		18-35M	PRE	160	74	46.3	38.3	54.3
			POST	160	153	95.6	91.2	98.2
A/Victoria/210/2009 (H3N2)	QIV2	6-17M	PRE	99	0	0.0	0.0	3.7
			POST	99	60	60.6	50.3	70.3
		18-35M	PRE	160	7	4.4	1.8	8.8
			POST	160	133	83.1	76.4	88.6
B/Brisbane/60/2008 (Victoria)	QIV2	6-17M	PRE	99	2	2.0	0.2	7.1
			POST	99	79	79.8	70.5	87.2
		18-35M	PRE	160	26	16.3	10.9	22.9
			POST	160	149	93.1	88.0	96.5
B/Florida/4/2006 (Yamagata)	QIV2	6-17M	PRE	99	0	0.0	0.0	3.7
			POST	99	94	94.9	88.6	98.3
		18-35M	PRE	160	22	13.8	8.8	20.1
			POST	160	156	97.5	93.7	99.3

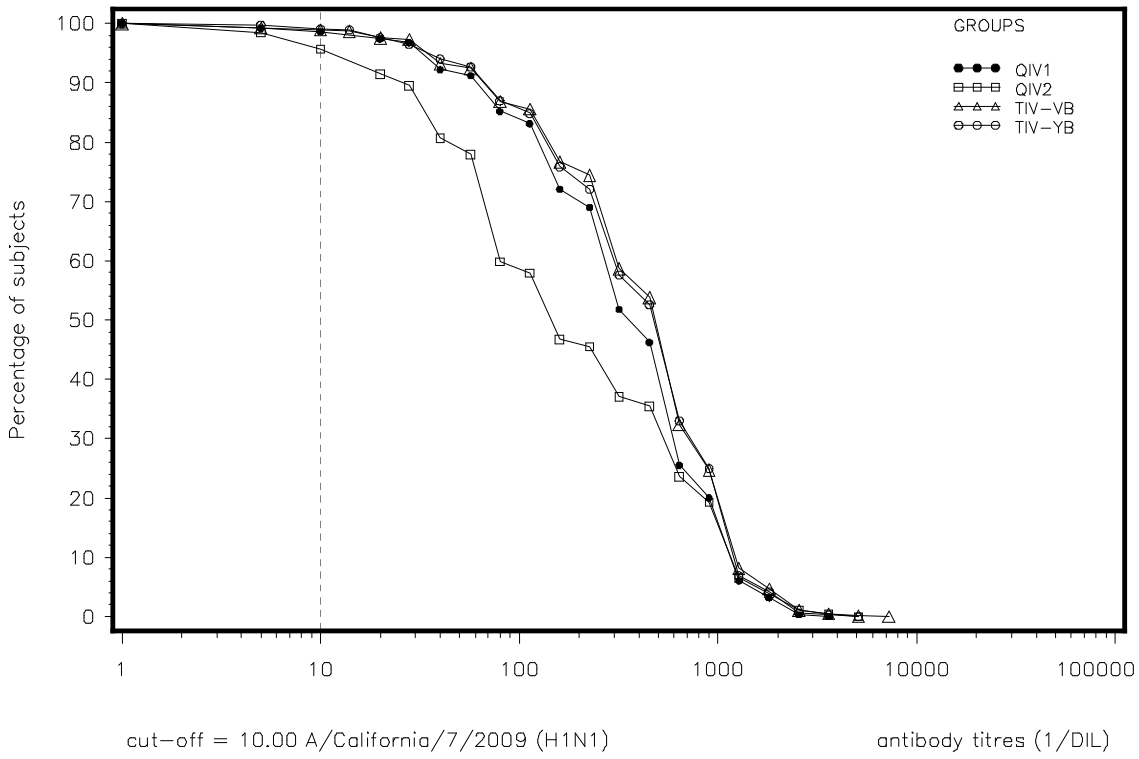
QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 35 Seroconversion Factor (SCF) for HI antibody titers post vaccination by age strata (3-17M/18-35M) (ATP cohort for immunogenicity)

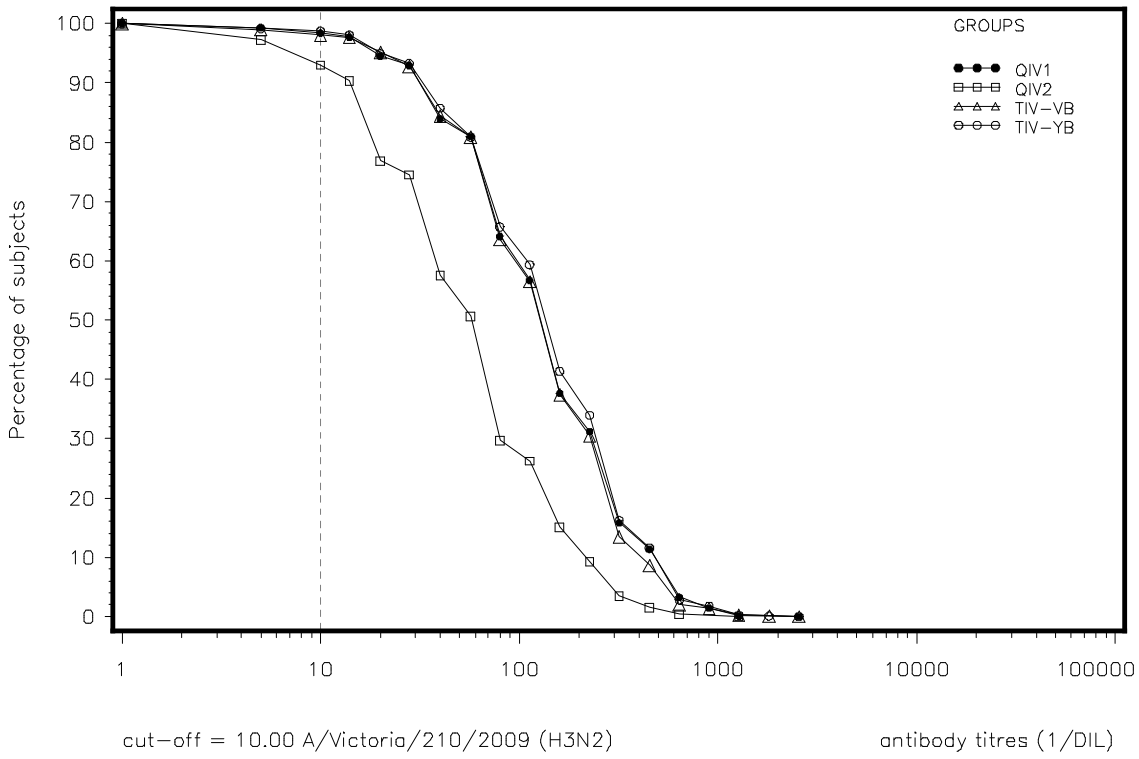
				SCF		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1) (1/DIL)	QIV2	6-17M	99	10.22	8.39	12.45
		18-35M	160	13.17	11.14	15.57
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV2	6-17M	99	8.05	6.49	9.98
		18-35M	160	13.23	11.38	15.38
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV2	6-17M	99	12.57	10.23	15.44
		18-35M	160	16.04	13.59	18.94
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV2	6-17M	99	23.60	19.48	28.59
		18-35M	160	25.78	21.82	30.45

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

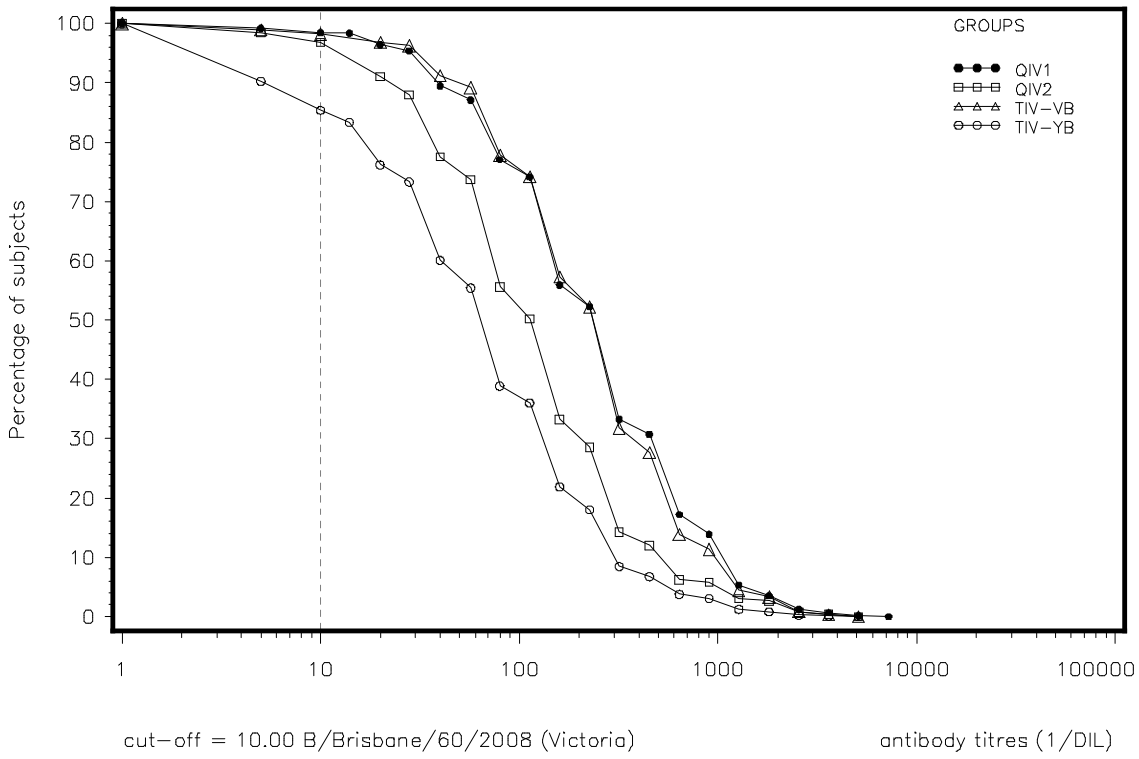
Supplement 36 **Reverse cumulative distribution curves for HI antibodies against Flu A/California/7/2009 (H1N1) at Day 28 post last vaccination (ATP-I)**



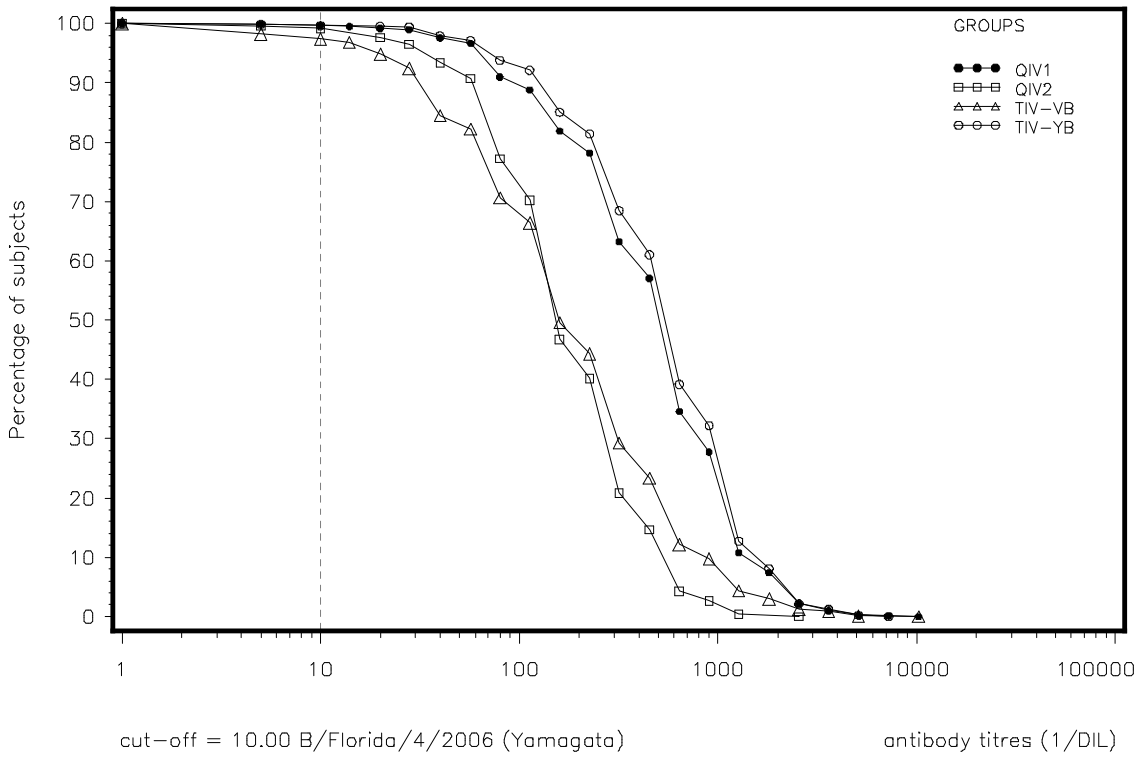
Supplement 37 **Reverse cumulative distribution curves for HI antibodies against Flu A/Victoria/210/2009 (H3N2) at Day 28 post last vaccination (ATP -I)**



Supplement 38 **Reverse cumulative distribution curves for HI antibodies against Flu B/Brisbane/60/2008 (Victoria) at Day 28 post last vaccination (ATP -I)**



Supplement 39 **Reverse cumulative distribution curves for HI antibodies against Flu B/Florida/4/2006 (Yamagata) at Day 28 post last vaccination (ATP-I)**



Supplement 40 Seropositivity rates and GMTs for HI antibody titers (Total vaccinated cohort)

				≥ 10 1/DIL				GMT				
						95% CI			95% CI			
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
A/California/7/2009 (H1N1)	QIV1	PRE	928	665	71.7	68.6	74.5	29.2	26.7	31.9	<10.0	1280.0
		POST	889	882	99.2	98.4	99.7	364.9	337.6	394.5	<10.0	3620.0
	TIV-VB	PRE	927	680	73.4	70.4	76.2	32.1	29.4	35.1	<10.0	1280.0
		POST	891	885	99.3	98.5	99.8	430.6	398.4	465.4	<10.0	7241.0
	TIV-YB	PRE	930	671	72.2	69.1	75.0	28.5	26.2	31.1	<10.0	1280.0
		POST	898	896	99.8	99.2	100	411.7	381.2	444.7	<10.0	5120.0
	QIV2	PRE	300	131	43.7	38.0	49.5	16.7	13.9	19.9	<10.0	640.0
		POST	277	272	98.2	95.8	99.4	195.5	163.1	234.2	<10.0	5120.0
A/Victoria/210/2009 (H3N2)	QIV1	PRE	928	600	64.7	61.5	67.7	18.0	16.6	19.6	<10.0	1280.0
		POST	889	883	99.3	98.5	99.8	143.8	134.3	154.0	<10.0	2560.0
	TIV-VB	PRE	927	607	65.5	62.3	68.5	18.7	17.2	20.3	<10.0	1280.0
		POST	891	881	98.9	97.9	99.5	140.0	131.0	149.6	<10.0	2560.0
	TIV-YB	PRE	928	599	64.5	61.4	67.6	19.4	17.9	21.2	<10.0	2560.0
		POST	898	891	99.2	98.4	99.7	149.5	139.8	160.0	<10.0	2560.0
	QIV2	PRE	300	22	7.3	4.7	10.9	5.7	5.4	6.1	<10.0	226.0
		POST	277	268	96.8	93.9	98.5	59.6	52.4	67.8	<10.0	1280.0
B/Brisbane/60/2008 (Victoria)	QIV1	PRE	928	618	66.6	63.5	69.6	24.5	22.3	27.0	<10.0	2560.0
		POST	889	882	99.2	98.4	99.7	250.5	230.9	271.8	<10.0	7241.0
	TIV-VB	PRE	927	631	68.1	65.0	71.1	25.6	23.4	28.1	<10.0	1810.0
		POST	891	882	99.0	98.1	99.5	244.7	226.4	264.5	<10.0	5120.0
	TIV-YB	PRE	929	644	69.3	66.2	72.3	25.4	23.2	27.9	<10.0	2560.0
		POST	897	810	90.3	88.2	92.2	67.4	61.4	74.0	<10.0	5120.0
	QIV2	PRE	300	83	27.7	22.7	33.1	8.3	7.3	9.5	<10.0	3620.0
		POST	277	272	98.2	95.8	99.4	126.3	109.0	146.3	<10.0	5120.0
B/Florida/4/2006 (Yamagata)	QIV1	PRE	928	754	81.3	78.6	83.7	57.7	52.0	64.0	<10.0	5120.0
		POST	889	888	99.9	99.4	100	513.7	479.0	550.8	<10.0	10240.0
	TIV-VB	PRE	927	759	81.9	79.2	84.3	56.9	51.3	63.0	<10.0	2560.0
		POST	891	876	98.3	97.2	99.1	195.4	179.4	212.8	<10.0	10240.0
	TIV-YB	PRE	930	767	82.5	79.9	84.9	64.5	58.2	71.4	<10.0	5120.0
		POST	898	897	99.9	99.4	100	571.8	534.6	611.5	<10.0	7241.0
	QIV2	PRE	300	81	27.0	22.1	32.4	7.6	6.9	8.3	<10.0	640.0
		POST	277	276	99.6	98.0	100	188.3	168.7	210.1	<10.0	2560.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST= Day 28 post last vaccination

Supplement 41 Seroconversion rate (SCR) for HI antibody titers post vaccination (Total vaccinated cohort)

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/California/7/2009 (H1N1)	QIV1	887	749	84.4	81.9	86.8
	TIV-VB	890	773	86.9	84.5	89.0
	TIV-YB	897	767	85.5	83.0	87.7
	QIV2	277	233	84.1	79.3	88.2
A/Victoria/210/2009 (H3N2)	QIV1	887	622	70.1	67.0	73.1
	TIV-VB	890	604	67.9	64.7	70.9
	TIV-YB	895	618	69.1	65.9	72.1
	QIV2	277	198	71.5	65.8	76.7
B/Brisbane/60/2008 (Victoria)	QIV1	887	663	74.7	71.8	77.6
	TIV-VB	890	640	71.9	68.8	74.8
	TIV-YB	895	266	29.7	26.7	32.8
	QIV2	277	234	84.5	79.7	88.5
B/Florida/4/2006 (Yamagata)	QIV1	887	669	75.4	72.5	78.2
	TIV-VB	890	372	41.8	38.5	45.1
	TIV-YB	897	660	73.6	70.6	76.4
	QIV2	277	260	93.9	90.4	96.4

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST= Day 28 post last vaccination

Supplement 42 Seroprotection rates for HI antibody titers (Total vaccinated cohort)

				SPR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	PRE	928	508	54.7	51.5	58.0
		POST	889	861	96.9	95.5	97.9
	TIV-VB	PRE	927	527	56.9	53.6	60.1
		POST	891	868	97.4	96.2	98.4
	TIV-YB	PRE	930	497	53.4	50.2	56.7
		POST	898	867	96.5	95.1	97.6
	QIV2	PRE	300	101	33.7	28.3	39.3
		POST	277	247	89.2	84.9	92.6
A/Victoria/210/2009 (H3N2)	QIV1	PRE	928	311	33.5	30.5	36.7
		POST	889	827	93.0	91.1	94.6
	TIV-VB	PRE	927	322	34.7	31.7	37.9
		POST	891	827	92.8	90.9	94.4
	TIV-YB	PRE	928	342	36.9	33.7	40.0
		POST	898	835	93.0	91.1	94.6
	QIV2	PRE	300	11	3.7	1.8	6.5
		POST	277	203	73.3	67.7	78.4
B/Brisbane/60/2008 (Victoria)	QIV1	PRE	928	408	44.0	40.7	47.2
		POST	889	849	95.5	93.9	96.8
	TIV-VB	PRE	927	429	46.3	43.0	49.5
		POST	891	858	96.3	94.8	97.4
	TIV-YB	PRE	929	420	45.2	42.0	48.5
		POST	897	656	73.1	70.1	76.0
	QIV2	PRE	300	29	9.7	6.6	13.6
		POST	277	243	87.7	83.3	91.3
B/Florida/4/2006 (Yamagata)	QIV1	PRE	928	610	65.7	62.6	68.8
		POST	889	880	99.0	98.1	99.5
	TIV-VB	PRE	927	613	66.1	63.0	69.2
		POST	891	824	92.5	90.5	94.1
	TIV-YB	PRE	930	652	70.1	67.1	73.0
		POST	898	892	99.3	98.6	99.8
	QIV2	PRE	300	23	7.7	4.9	11.3
		POST	277	267	96.4	93.5	98.3

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST= Day 28 post last vaccination

Supplement 43 Seroconversion Factor (SCF) for HI antibody titers post last vaccination (Total vaccinated cohort)

			SCF		
				95% CI	
Strain	**Group**	**N**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1) (1/DIL)	QIV1	887	12.28	11.33	13.32
	TIV-VB	890	13.33	12.30	14.43
	TIV-YB	897	14.41	13.28	15.63
	QIV2	277	11.73	10.37	13.28
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	887	7.95	7.31	8.64
	TIV-VB	890	7.37	6.79	8.01
	TIV-YB	895	7.65	7.04	8.31
	QIV2	277	10.49	9.28	11.86
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	887	10.19	9.30	11.16
	TIV-VB	890	9.60	8.74	10.54
	TIV-YB	895	2.63	2.47	2.80
	QIV2	277	14.59	12.88	16.53
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	887	8.86	8.12	9.65
	TIV-VB	890	3.40	3.17	3.65
	TIV-YB	897	8.77	8.05	9.56
	QIV2	277	24.25	21.48	27.38

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 44 Seropositivity rates and GMTs for HI antibody titers by age strata (3-8y/9-17y) (Total vaccinated cohort)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)	QIV1	3-8y	PRE	465	302	64.9	60.4	69.3	24.7	21.8	28.1
			POST	435	431	99.1	97.7	99.7	315.4	279.8	355.6
		9-17y	PRE	463	363	78.4	74.4	82.1	34.5	30.5	39.0
			POST	454	451	99.3	98.1	99.9	419.6	380.0	463.4
	TIV-VB	3-8y	PRE	461	305	66.2	61.6	70.5	27.3	23.9	31.0
			POST	436	433	99.3	98.0	99.9	389.4	346.2	438.0
		9-17y	PRE	465	375	80.6	76.8	84.1	37.9	33.6	42.7
			POST	455	452	99.3	98.1	99.9	474.1	428.1	525.0
	TIV-YB	3-8y	PRE	462	304	65.8	61.3	70.1	23.7	21.0	26.8
			POST	437	435	99.5	98.4	99.9	347.0	308.6	390.1
		9-17y	PRE	468	367	78.4	74.4	82.1	34.2	30.4	38.5
			POST	461	461	100	99.2	100	484.2	438.4	534.7
A/Victoria/210/2009 (H3N2)	QIV1	3-8y	PRE	465	294	63.2	58.7	67.6	19.3	17.1	21.8
			POST	435	430	98.9	97.3	99.6	138.7	124.3	154.8
		9-17y	PRE	463	306	66.1	61.6	70.4	16.8	15.1	18.8
			POST	454	453	99.8	98.8	100	148.9	137.1	161.8
	TIV-VB	3-8y	PRE	461	288	62.5	57.9	66.9	20.5	18.0	23.2
			POST	436	430	98.6	97.0	99.5	145.7	132.0	160.8
		9-17y	PRE	465	319	68.6	64.2	72.8	17.2	15.4	19.1
			POST	455	451	99.1	97.8	99.8	134.8	123.2	147.5
	TIV-YB	3-8y	PRE	460	285	62.0	57.3	66.4	19.9	17.5	22.5
			POST	437	431	98.6	97.0	99.5	146.0	131.7	162.0
		9-17y	PRE	468	314	67.1	62.6	71.3	19.0	17.0	21.3
			POST	461	460	99.8	98.8	100	153.0	140.0	167.1
B/Brisbane/60/2008 (Victoria)	QIV1	3-8y	PRE	465	254	54.6	50.0	59.2	18.3	16.0	20.9
			POST	435	429	98.6	97.0	99.5	195.7	172.8	221.7
		9-17y	PRE	463	364	78.6	74.6	82.3	33.0	29.1	37.4
			POST	454	453	99.8	98.8	100	317.3	286.7	351.2
	TIV-VB	3-8y	PRE	461	264	57.3	52.6	61.8	20.0	17.4	22.9
			POST	436	429	98.4	96.7	99.4	196.3	175.1	220.0
		9-17y	PRE	465	366	78.7	74.7	82.3	32.9	29.1	37.1
			POST	455	453	99.6	98.4	99.9	302.2	272.7	335.0
	TIV-YB	3-8y	PRE	461	261	56.6	52.0	61.2	18.3	16.1	21.0
			POST	436	372	85.3	81.6	88.5	52.6	45.4	61.0
		9-17y	PRE	468	383	81.8	78.0	85.2	35.1	31.0	39.6
			POST	461	438	95.0	92.6	96.8	85.3	76.2	95.4
B/Florida/4/2006 (Yamagata)	QIV1	3-8y	PRE	465	318	68.4	63.9	72.6	28.0	24.4	32.1
			POST	435	434	99.8	98.7	100	367.9	332.3	407.3
		9-17y	PRE	463	436	94.2	91.6	96.1	119.2	104.9	135.5
			POST	454	454	100	99.2	100	707.3	648.7	771.2
	TIV-VB	3-8y	PRE	461	324	70.3	65.9	74.4	28.6	24.9	32.8
			POST	436	422	96.8	94.7	98.2	102.6	91.4	115.3
		9-17y	PRE	465	434	93.3	90.7	95.4	112.0	98.8	127.0
			POST	455	454	99.8	98.8	100	362.0	329.2	398.1
	TIV-YB	3-8y	PRE	462	313	67.7	63.3	72.0	29.1	25.4	33.4
			POST	437	436	99.8	98.7	100	408.2	367.2	453.8
		9-17y	PRE	468	454	97.0	95.0	98.4	141.3	126.3	158.0

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
			POST	461	461	100	99.2	100	787.0	731.4	846.8

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 45 Seroconversion rate (SCR) for HI antibody titers post last vaccination by age strata (3-8y/9-17y) (Total vaccinated cohort)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	3-8y	433	383	88.5	85.1	91.3
		9-17y	454	366	80.6	76.7	84.2
	TIV-VB	3-8y	435	402	92.4	89.5	94.7
		9-17y	455	371	81.5	77.7	85.0
	TIV-YB	3-8y	437	391	89.5	86.2	92.2
		9-17y	460	376	81.7	77.9	85.2
A/Victoria/210/2009 (H3N2)	QIV1	3-8y	433	299	69.1	64.5	73.4
		9-17y	454	323	71.1	66.7	75.3
	TIV-VB	3-8y	435	292	67.1	62.5	71.5
		9-17y	455	312	68.6	64.1	72.8
	TIV-YB	3-8y	435	300	69.0	64.4	73.3
		9-17y	460	318	69.1	64.7	73.3
B/Brisbane/60/2008 (Victoria)	QIV1	3-8y	433	338	78.1	73.9	81.9
		9-17y	454	325	71.6	67.2	75.7
	TIV-VB	3-8y	435	338	77.7	73.5	81.5
		9-17y	455	302	66.4	61.8	70.7
	TIV-YB	3-8y	435	136	31.3	26.9	35.9
		9-17y	460	130	28.3	24.2	32.6
B/Florida/4/2006 (Yamagata)	QIV1	3-8y	433	376	86.8	83.3	89.9
		9-17y	454	293	64.5	59.9	68.9
	TIV-VB	3-8y	435	190	43.7	39.0	48.5
		9-17y	455	182	40.0	35.5	44.7
	TIV-YB	3-8y	437	384	87.9	84.4	90.8
		9-17y	460	276	60.0	55.4	64.5

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 46 Seroprotection rates for HI antibody titers by age strata (3-8y/9-17y) (Total vaccinated cohort)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	3-8y	PRE	465	232	49.9	45.3	54.5
			POST	435	415	95.4	93.0	97.2
		9-17y	PRE	463	276	59.6	55.0	64.1
			POST	454	446	98.2	96.6	99.2
	TIV-VB	3-8y	PRE	461	239	51.8	47.2	56.5
			POST	436	424	97.2	95.2	98.6
		9-17y	PRE	465	288	61.9	57.4	66.4
			POST	455	444	97.6	95.7	98.8
	TIV-YB	3-8y	PRE	462	220	47.6	43.0	52.3
			POST	437	417	95.4	93.0	97.2
		9-17y	PRE	468	277	59.2	54.6	63.7
			POST	461	450	97.6	95.8	98.8
A/Victoria/210/2009 (H3N2)	QIV1	3-8y	PRE	465	175	37.6	33.2	42.2
			POST	435	389	89.4	86.1	92.2
		9-17y	PRE	463	136	29.4	25.3	33.8
			POST	454	438	96.5	94.3	98.0
	TIV-VB	3-8y	PRE	461	187	40.6	36.0	45.2
			POST	436	402	92.2	89.3	94.5
		9-17y	PRE	465	135	29.0	24.9	33.4
			POST	455	425	93.4	90.7	95.5
	TIV-YB	3-8y	PRE	460	177	38.5	34.0	43.1
			POST	437	398	91.1	88.0	93.6
		9-17y	PRE	468	165	35.3	30.9	39.8
			POST	461	437	94.8	92.4	96.6
B/Brisbane/60/2008 (Victoria)	QIV1	3-8y	PRE	465	159	34.2	29.9	38.7
			POST	435	408	93.8	91.1	95.9
		9-17y	PRE	463	249	53.8	49.1	58.4
			POST	454	441	97.1	95.2	98.5
	TIV-VB	3-8y	PRE	461	176	38.2	33.7	42.8
			POST	436	418	95.9	93.6	97.5
		9-17y	PRE	465	253	54.4	49.8	59.0
			POST	455	440	96.7	94.6	98.1
	TIV-YB	3-8y	PRE	461	161	34.9	30.6	39.5
			POST	436	280	64.2	59.5	68.7
		9-17y	PRE	468	259	55.3	50.7	59.9
			POST	461	376	81.6	77.7	85.0
B/Florida/4/2006 (Yamagata)	QIV1	3-8y	PRE	465	227	48.8	44.2	53.5
			POST	435	429	98.6	97.0	99.5
		9-17y	PRE	463	383	82.7	79.0	86.1
			POST	454	451	99.3	98.1	99.9
	TIV-VB	3-8y	PRE	461	224	48.6	43.9	53.3
			POST	436	372	85.3	81.6	88.5
		9-17y	PRE	465	388	83.4	79.7	86.7
			POST	455	452	99.3	98.1	99.9
	TIV-YB	3-8y	PRE	462	236	51.1	46.4	55.7
			POST	437	432	98.9	97.4	99.6
		9-17y	PRE	468	416	88.9	85.7	91.6
			POST	461	460	99.8	98.8	100

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 47 Seroconversion Factor (SCF) for HI antibody titers post vaccination by age strata (3-8y/9-17y) (Total vaccinated cohort)

				SCF		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1) (1/DIL)	QIV1	3-8y	433	12.48	11.30	13.77
		9-17y	454	12.10	10.66	13.74
	TIV-VB	3-8y	435	14.32	12.95	15.84
		9-17y	455	12.44	11.00	14.06
	TIV-YB	3-8y	437	14.60	13.26	16.07
		9-17y	460	14.23	12.49	16.21
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	3-8y	433	7.07	6.34	7.88
		9-17y	454	8.89	7.83	10.09
	TIV-VB	3-8y	435	6.91	6.18	7.73
		9-17y	455	7.85	6.94	8.87
	TIV-YB	3-8y	435	7.13	6.38	7.97
		9-17y	460	8.18	7.24	9.23
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	3-8y	433	10.80	9.57	12.18
		9-17y	454	9.64	8.41	11.04
	TIV-VB	3-8y	435	9.90	8.77	11.18
		9-17y	455	9.32	8.08	10.74
	TIV-YB	3-8y	435	2.85	2.58	3.15
		9-17y	460	2.43	2.24	2.64
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	3-8y	433	13.17	11.71	14.81
		9-17y	454	6.07	5.40	6.81
	TIV-VB	3-8y	435	3.54	3.22	3.89
		9-17y	455	3.27	2.95	3.63
	TIV-YB	3-8y	437	13.93	12.44	15.60
		9-17y	460	5.65	5.04	6.35

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 48 Seropositivity rates and GMTs for HI antibody titers by previous influenza vaccination status (Total vaccinated cohort)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	346	203	58.7	53.3	63.9	22.9	19.7	26.7
			POST	317	315	99.4	97.7	99.9	323.9	281.9	372.1
		prim	PRE	582	462	79.4	75.9	82.6	33.7	30.3	37.6
			POST	572	567	99.1	98.0	99.7	389.9	355.1	428.0
	TIV-VB	Unprm	PRE	339	216	63.7	58.3	68.8	27.0	23.1	31.5
			POST	318	316	99.4	97.7	99.9	407.1	355.5	466.2
		prim	PRE	588	464	78.9	75.4	82.1	35.5	31.8	39.5
			POST	573	569	99.3	98.2	99.8	444.2	404.0	488.4
	TIV-YB	Unprm	PRE	336	210	62.5	57.1	67.7	23.7	20.4	27.4
			POST	316	314	99.4	97.7	99.9	380.9	332.5	436.4
		prim	PRE	594	461	77.6	74.0	80.9	31.7	28.5	35.2
			POST	582	582	100	99.4	100	429.4	391.1	471.5
	QIV2	Unprm	PRE	241	86	35.7	29.6	42.1	14.9	12.2	18.3
			POST	222	217	97.7	94.8	99.3	164.6	134.3	201.6
		prim	PRE	59	45	76.3	63.4	86.4	26.0	18.4	36.8
			POST	55	55	100	93.5	100	391.5	275.2	556.8
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	346	218	63.0	57.7	68.1	19.2	16.7	22.1
			POST	317	315	99.4	97.7	99.9	146.7	129.9	165.8
		prim	PRE	582	382	65.6	61.6	69.5	17.4	15.7	19.2
			POST	572	568	99.3	98.2	99.8	142.2	131.1	154.4
	TIV-VB	Unprm	PRE	339	216	63.7	58.3	68.8	20.2	17.5	23.3
			POST	318	317	99.7	98.3	100	156.4	140.5	174.1
		prim	PRE	588	391	66.5	62.5	70.3	17.9	16.2	19.8
			POST	573	564	98.4	97.0	99.3	131.7	121.0	143.3
	TIV-YB	Unprm	PRE	334	206	61.7	56.2	66.9	19.6	17.0	22.7
			POST	316	314	99.4	97.7	99.9	163.7	145.9	183.8
		prim	PRE	594	393	66.2	62.2	70.0	19.3	17.4	21.5
			POST	582	577	99.1	98.0	99.7	142.4	131.0	154.8
	QIV2	Unprm	PRE	241	16	6.6	3.8	10.6	5.8	5.4	6.2
			POST	222	214	96.4	93.0	98.4	57.7	49.8	66.8
		prim	PRE	59	6	10.2	3.8	20.8	5.6	5.1	6.1
			POST	55	54	98.2	90.3	100	67.9	52.0	88.7
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	346	180	52.0	46.6	57.4	17.7	15.2	20.7
			POST	317	316	99.7	98.3	100	217.8	190.4	249.2
		prim	PRE	582	438	75.3	71.5	78.7	29.8	26.6	33.5
			POST	572	566	99.0	97.7	99.6	270.7	244.5	299.8
	TIV-VB	Unprm	PRE	339	187	55.2	49.7	60.5	19.5	16.7	22.9
			POST	318	316	99.4	97.7	99.9	222.9	195.9	253.6
		prim	PRE	588	444	75.5	71.8	78.9	30.0	26.8	33.5
			POST	573	566	98.8	97.5	99.5	257.7	233.8	284.1
	TIV-YB	Unprm	PRE	335	180	53.7	48.2	59.2	18.1	15.4	21.2
			POST	315	259	82.2	77.5	86.3	51.3	42.7	61.6
		prim	PRE	594	464	78.1	74.6	81.4	30.8	27.6	34.5
			POST	582	551	94.7	92.5	96.4	78.2	70.6	86.7
	QIV2	Unprm	PRE	241	50	20.7	15.8	26.4	7.3	6.5	8.3
			POST	222	217	97.7	94.8	99.3	115.6	98.2	136.2
		prim	PRE	59	33	55.9	42.4	68.8	14.3	9.8	20.9
			POST	55	55	100	93.5	100	180.3	129.6	250.8

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	346	222	64.2	58.9	69.2	27.0	22.9	31.7
			POST	317	317	100	98.8	100	384.5	344.6	429.0
		prim	PRE	582	532	91.4	88.8	93.6	90.6	80.2	102.4
			POST	572	571	99.8	99.0	100	603.1	552.6	658.2
	TIV-VB	Unprm	PRE	339	226	66.7	61.4	71.7	27.4	23.3	32.3
			POST	318	306	96.2	93.5	98.0	97.2	84.4	111.9
		prim	PRE	588	533	90.6	88.0	92.9	86.6	76.9	97.5
			POST	573	570	99.5	98.5	99.9	287.8	262.1	316.1
	TIV-YB	Unprm	PRE	336	218	64.9	59.5	70.0	28.1	23.8	33.2
			POST	316	316	100	98.8	100	445.7	396.5	501.0
		prim	PRE	594	549	92.4	90.0	94.4	103.1	92.1	115.5
			POST	582	581	99.8	99.0	100	654.7	604.3	709.2
	QIV2	Unprm	PRE	241	47	19.5	14.7	25.1	6.4	5.9	6.8
			POST	222	222	100	98.4	100	184.7	165.2	206.5
		prim	PRE	59	34	57.6	44.1	70.4	15.5	11.3	21.3
			POST	55	54	98.2	90.3	100	203.3	146.1	282.8

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 49 Seroconversion rate (SCR) for HI antibody titers post last vaccination by previous influenza vaccination status (Total vaccinated cohort)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	315	285	90.5	86.7	93.5
		prim	572	464	81.1	77.7	84.2
	TIV-VB	Unprm	318	298	93.7	90.5	96.1
		prim	572	475	83.0	79.7	86.0
	TIV-YB	Unprm	316	291	92.1	88.5	94.8
		prim	581	476	81.9	78.6	85.0
	QIV2	Unprm	222	182	82.0	76.3	86.8
		prim	55	51	92.7	82.4	98.0
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	315	223	70.8	65.4	75.8
		prim	572	399	69.8	65.8	73.5
	TIV-VB	Unprm	318	228	71.7	66.4	76.6
		prim	572	376	65.7	61.7	69.6
	TIV-YB	Unprm	314	233	74.2	69.0	79.0
		prim	581	385	66.3	62.3	70.1
	QIV2	Unprm	222	157	70.7	64.3	76.6
		prim	55	41	74.5	61.0	85.3
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	315	258	81.9	77.2	86.0
		prim	572	405	70.8	66.9	74.5
	TIV-VB	Unprm	318	260	81.8	77.1	85.8
		prim	572	380	66.4	62.4	70.3
	TIV-YB	Unprm	314	97	30.9	25.8	36.3
		prim	581	169	29.1	25.4	33.0
	QIV2	Unprm	222	187	84.2	78.8	88.8
		prim	55	47	85.5	73.3	93.5
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	315	277	87.9	83.8	91.3
		prim	572	392	68.5	64.5	72.3
	TIV-VB	Unprm	318	137	43.1	37.6	48.7
		prim	572	235	41.1	37.0	45.2
	TIV-YB	Unprm	316	283	89.6	85.6	92.7
		prim	581	377	64.9	60.9	68.8
	QIV2	Unprm	222	214	96.4	93.0	98.4
		prim	55	46	83.6	71.2	92.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 50 Seroprotection rates for HI antibody titers by previous influenza vaccination status (Total vaccinated cohort)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	346	169	48.8	43.5	54.2
			POST	317	304	95.9	93.1	97.8
		prim	PRE	582	339	58.2	54.1	62.3
			POST	572	557	97.4	95.7	98.5
	TIV-VB	Unprm	PRE	339	182	53.7	48.2	59.1
			POST	318	309	97.2	94.7	98.7
		prim	PRE	588	345	58.7	54.6	62.7
			POST	573	559	97.6	95.9	98.7
	TIV-YB	Unprm	PRE	336	169	50.3	44.8	55.8
			POST	316	304	96.2	93.5	98.0
		prim	PRE	594	328	55.2	51.1	59.3
			POST	582	563	96.7	94.9	98.0
	QIV2	Unprm	PRE	241	76	31.5	25.7	37.8
			POST	222	194	87.4	82.3	91.5
		prim	PRE	59	25	42.4	29.6	55.9
			POST	55	53	96.4	87.5	99.6
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	346	128	37.0	31.9	42.3
			POST	317	289	91.2	87.5	94.1
		prim	PRE	582	183	31.4	27.7	35.4
			POST	572	538	94.1	91.8	95.8
	TIV-VB	Unprm	PRE	339	138	40.7	35.4	46.1
			POST	318	299	94.0	90.8	96.4
		prim	PRE	588	184	31.3	27.6	35.2
			POST	573	528	92.1	89.6	94.2
	TIV-YB	Unprm	PRE	334	129	38.6	33.4	44.1
			POST	316	295	93.4	90.0	95.8
		prim	PRE	594	213	35.9	32.0	39.9
			POST	582	540	92.8	90.4	94.7
	QIV2	Unprm	PRE	241	11	4.6	2.3	8.0
			POST	222	162	73.0	66.6	78.7
		prim	PRE	59	0	0.0	0.0	6.1
			POST	55	41	74.5	61.0	85.3
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	346	118	34.1	29.1	39.4
			POST	317	304	95.9	93.1	97.8
		prim	PRE	582	290	49.8	45.7	54.0
			POST	572	545	95.3	93.2	96.9
	TIV-VB	Unprm	PRE	339	129	38.1	32.9	43.5
			POST	318	311	97.8	95.5	99.1
		prim	PRE	588	300	51.0	46.9	55.1
			POST	573	547	95.5	93.4	97.0
	TIV-YB	Unprm	PRE	335	117	34.9	29.8	40.3
			POST	315	195	61.9	56.3	67.3
		prim	PRE	594	303	51.0	46.9	55.1
			POST	582	461	79.2	75.7	82.4
	QIV2	Unprm	PRE	241	16	6.6	3.8	10.6
			POST	222	192	86.5	81.3	90.7
		prim	PRE	59	13	22.0	12.3	34.7
			POST	55	51	92.7	82.4	98.0

					SPR			
							95% CI	
Strain	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	346	168	48.6	43.2	54.0
			POST	317	316	99.7	98.3	100
		prim	PRE	582	442	75.9	72.3	79.4
			POST	572	564	98.6	97.3	99.4
	TIV-VB	Unprm	PRE	339	158	46.6	41.2	52.1
			POST	318	265	83.3	78.8	87.3
		prim	PRE	588	455	77.4	73.8	80.7
			POST	573	559	97.6	95.9	98.7
	TIV-YB	Unprm	PRE	336	167	49.7	44.2	55.2
			POST	316	314	99.4	97.7	99.9
		prim	PRE	594	485	81.6	78.3	84.7
			POST	582	578	99.3	98.2	99.8
	QIV2	Unprm	PRE	241	8	3.3	1.4	6.4
			POST	222	217	97.7	94.8	99.3
		prim	PRE	59	15	25.4	15.0	38.4
			POST	55	50	90.9	80.0	97.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 51 Seroconversion Factor (SCF) for HI antibody titers post last vaccination by previous influenza vaccination status (Total vaccinated cohort)

				SCF		
					95% CI	
Strain	Group	Sub-group	N	Value	LL	UL
A/California/7/2009 (H1N1) (1/DIL)	QIV1	Unprm	315	13.86	12.40	15.48
		prim	572	11.49	10.30	12.82
	TIV-VB	Unprm	318	15.22	13.59	17.04
		prim	572	12.38	11.13	13.77
	TIV-YB	Unprm	316	16.00	14.37	17.82
		prim	581	13.61	12.17	15.21
	QIV2	Unprm	222	11.14	9.72	12.76
		prim	55	14.47	10.74	19.51
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	Unprm	315	7.50	6.60	8.52
		prim	572	8.21	7.36	9.15
	TIV-VB	Unprm	318	7.48	6.60	8.47
		prim	572	7.32	6.56	8.16
	TIV-YB	Unprm	314	8.01	7.05	9.10
		prim	581	7.46	6.70	8.30
	QIV2	Unprm	222	10.14	8.82	11.66
		prim	55	12.06	9.29	15.66
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	Unprm	315	12.46	10.83	14.33
		prim	572	9.12	8.10	10.26
	TIV-VB	Unprm	318	11.49	9.99	13.22
		prim	572	8.68	7.68	9.82
	TIV-YB	Unprm	314	2.84	2.51	3.21
		prim	581	2.52	2.34	2.71
	QIV2	Unprm	222	15.34	13.34	17.64
		prim	55	11.90	8.98	15.77
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	Unprm	315	14.34	12.47	16.48
		prim	572	6.79	6.12	7.53
	TIV-VB	Unprm	318	3.52	3.15	3.92
		prim	572	3.34	3.05	3.66
	TIV-YB	Unprm	316	15.90	13.87	18.23
		prim	581	6.35	5.74	7.02
	QIV2	Unprm	222	28.61	25.20	32.48
		prim	55	12.44	9.42	16.44

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 52 Seropositivity rates and GMTs for HI antibody titers by age strata (3-17M/18-35M) (Total vaccinated cohort)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL
A/California/7/2009 (H1N1)	QIV2	6-17M	PRE	119	21	17.6	11.3	25.7	8.3	6.7	10.4
			POST	106	103	97.2	92.0	99.4	86.8	66.8	112.8
		18-35M	PRE	181	110	60.8	53.3	67.9	26.2	20.8	33.2
			POST	171	169	98.8	95.8	99.9	323.3	261.4	399.9
A/Victoria/210/2009 (H3N2)	QIV2	6-17M	PRE	119	1	0.8	0.0	4.6	5.0	5.0	5.1
			POST	106	99	93.4	86.9	97.3	39.6	32.2	48.6
		18-35M	PRE	181	21	11.6	7.3	17.2	6.3	5.6	6.9
			POST	171	169	98.8	95.8	99.9	76.8	65.9	89.6
B/Brisbane/60/2008 (Victoria)	QIV2	6-17M	PRE	119	12	10.1	5.3	17.0	5.7	5.2	6.2
			POST	106	102	96.2	90.6	99.0	74.4	60.2	92.0
		18-35M	PRE	181	71	39.2	32.1	46.7	10.8	8.9	13.1
			POST	171	170	99.4	96.8	100	175.3	145.8	210.6
B/Florida/4/2006 (Yamagata)	QIV2	6-17M	PRE	119	17	14.3	8.5	21.9	5.7	5.4	6.1
			POST	106	106	100	96.6	100	131.5	111.7	154.9
		18-35M	PRE	181	64	35.4	28.4	42.8	9.1	7.9	10.5
			POST	171	170	99.4	96.8	100	235.2	205.1	269.7

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 53 Seroconversion rate (SCR) for HI antibody titers post last vaccination by age strata (3-17M/18-35M) (Total vaccinated cohort)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV2	6-17M	106	82	77.4	68.2	84.9
		18-35M	171	151	88.3	82.5	92.7
A/Victoria/210/2009 (H3N2)	QIV2	6-17M	106	63	59.4	49.5	68.9
		18-35M	171	135	78.9	72.1	84.8
B/Brisbane/60/2008 (Victoria)	QIV2	6-17M	106	86	81.1	72.4	88.1
		18-35M	171	148	86.5	80.5	91.3
B/Florida/4/2006 (Yamagata)	QIV2	6-17M	106	99	93.4	86.9	97.3
		18-35M	171	161	94.2	89.5	97.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 54 Seroprotection rates for HI antibody titers by age strata (3-17M/18-35M) (Total vaccinated cohort)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV2	6-17M	PRE	119	16	13.4	7.9	20.9
			POST	106	85	80.2	71.3	87.3
		18-35M	PRE	181	85	47.0	39.5	54.5
			POST	171	162	94.7	90.2	97.6
A/Victoria/210/2009 (H3N2)	QIV2	6-17M	PRE	119	0	0.0	0.0	3.1
			POST	106	63	59.4	49.5	68.9
		18-35M	PRE	181	11	6.1	3.1	10.6
			POST	171	140	81.9	75.3	87.3
B/Brisbane/60/2008 (Victoria)	QIV2	6-17M	PRE	119	2	1.7	0.2	5.9
			POST	106	86	81.1	72.4	88.1
		18-35M	PRE	181	27	14.9	10.1	21.0
			POST	171	157	91.8	86.6	95.5
B/Florida/4/2006 (Yamagata)	QIV2	6-17M	PRE	119	0	0.0	0.0	3.1
			POST	106	100	94.3	88.1	97.9
		18-35M	PRE	181	23	12.7	8.2	18.5
			POST	171	167	97.7	94.1	99.4

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 55 Seroconversion Factor (SCF) for HI antibody titers post vaccination by age strata (3-17M/18-35M) (Total vaccinated cohort)

				SCF		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1) (1/DIL)	QIV2	6-17M	106	10.39	8.62	12.52
		18-35M	171	12.65	10.73	14.91
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV2	6-17M	106	7.86	6.39	9.67
		18-35M	171	12.55	10.84	14.54
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV2	6-17M	106	13.02	10.70	15.85
		18-35M	171	15.65	13.31	18.41
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV2	6-17M	106	22.64	18.70	27.40
		18-35M	171	25.31	21.60	29.65

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
6-17M = Subjects aged between 6 months to 17 months
18-35M = Subjects aged between 18 months to 35 months
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 56 Seropositivity rates and GMTs for HI antibody titers by previous influenza vaccination status for subjects aged between 3 to 8 years old (Total vaccinated cohort)

					≥ 10 1/DIL				GMT				
							95% CI			95% CI			
Antibody	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	346	203	58.7	53.3	63.9	22.9	19.7	26.7	<10.0	1280.0
			POST	317	315	99.4	97.7	99.9	323.9	281.9	372.1	<10.0	3620.0
		prim	PRE	119	99	83.2	75.2	89.4	30.9	24.6	38.8	<10.0	640.0
			POST	118	116	98.3	94.0	99.8	293.8	231.4	373.2	<10.0	2560.0
	TIV-VB	Unprm	PRE	338	216	63.9	58.5	69.0	27.1	23.3	31.6	<10.0	905.0
			POST	318	316	99.4	97.7	99.9	407.1	355.5	466.2	<10.0	5120.0
		prim	PRE	123	89	72.4	63.6	80.0	27.6	21.7	35.2	<10.0	320.0
			POST	118	117	99.2	95.4	100	345.4	272.5	437.9	<10.0	7241.0
	TIV-YB	Unprm	PRE	335	210	62.7	57.3	67.9	23.8	20.5	27.5	<10.0	640.0
			POST	315	313	99.4	97.7	99.9	381.2	332.6	436.8	<10.0	5120.0
		prim	PRE	127	94	74.0	65.5	81.4	23.5	18.9	29.4	<10.0	640.0
			POST	122	122	100	97.0	100	272.2	217.3	341.0	10.0	5120.0
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	346	218	63.0	57.7	68.1	19.2	16.7	22.1	<10.0	1280.0
			POST	317	315	99.4	97.7	99.9	146.7	129.9	165.8	<10.0	1280.0
		prim	PRE	119	76	63.9	54.6	72.5	19.6	15.5	25.0	<10.0	1280.0
			POST	118	115	97.5	92.7	99.5	119.3	94.0	151.2	<10.0	2560.0
	TIV-VB	Unprm	PRE	338	216	63.9	58.5	69.0	20.3	17.6	23.4	<10.0	905.0
			POST	318	317	99.7	98.3	100	156.4	140.5	174.1	<10.0	1810.0
		prim	PRE	123	72	58.5	49.3	67.3	20.9	15.9	27.5	<10.0	1280.0
			POST	118	113	95.8	90.4	98.6	120.3	96.4	150.2	<10.0	1280.0
	TIV-YB	Unprm	PRE	333	206	61.9	56.4	67.1	19.7	17.0	22.8	<10.0	1810.0
			POST	315	313	99.4	97.7	99.9	163.7	145.8	183.8	<10.0	1280.0
		prim	PRE	127	79	62.2	53.2	70.7	20.4	15.8	26.3	<10.0	2560.0
			POST	122	118	96.7	91.8	99.1	108.7	87.8	134.5	<10.0	1280.0
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	346	180	52.0	46.6	57.4	17.7	15.2	20.7	<10.0	905.0
			POST	317	316	99.7	98.3	100	217.8	190.4	249.2	<10.0	5120.0
		prim	PRE	119	74	62.2	52.8	70.9	20.1	15.3	26.4	<10.0	2560.0
			POST	118	113	95.8	90.4	98.6	146.9	111.1	194.4	<10.0	5120.0
	TIV-VB	Unprm	PRE	338	186	55.0	49.6	60.4	19.6	16.7	23.0	<10.0	1810.0
			POST	318	316	99.4	97.7	99.9	222.9	195.9	253.6	<10.0	5120.0
		prim	PRE	123	78	63.4	54.3	71.9	21.1	16.3	27.3	<10.0	640.0
			POST	118	113	95.8	90.4	98.6	139.4	110.9	175.2	<10.0	5120.0
	TIV-YB	Unprm	PRE	334	180	53.9	48.4	59.3	18.1	15.5	21.2	<10.0	2560.0
			POST	314	258	82.2	77.5	86.2	51.4	42.8	61.8	<10.0	5120.0
		prim	PRE	127	81	63.8	54.8	72.1	18.9	14.8	24.2	<10.0	905.0
			POST	122	114	93.4	87.5	97.1	55.8	43.9	70.9	<10.0	1810.0
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	346	222	64.2	58.9	69.2	27.0	22.9	31.7	<10.0	1280.0
			POST	317	317	100	98.8	100	384.5	344.6	429.0	28.0	5120.0
		prim	PRE	119	96	80.7	72.4	87.3	31.2	24.3	40.1	<10.0	640.0
			POST	118	117	99.2	95.4	100	326.7	258.5	412.9	<10.0	3620.0
	TIV-VB	Unprm	PRE	338	225	66.6	61.3	71.6	27.2	23.1	32.1	<10.0	1280.0
			POST	318	306	96.2	93.5	98.0	97.2	84.4	111.9	<10.0	10240.0
		prim	PRE	123	99	80.5	72.4	87.1	32.7	25.8	41.6	<10.0	1280.0
			POST	118	116	98.3	94.0	99.8	118.9	97.1	145.5	<10.0	2560.0

					≥ 10 1/DIL				GMT				
							95% CI			95% CI			
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
	TIV-YB	Unprm	PRE	335	217	64.8	59.4	69.9	28.0	23.7	33.0	<10.0	5120.0
			POST	315	315	100	98.8	100	443.2	394.4	498.1	10.0	5120.0
		prim	PRE	127	96	75.6	67.2	82.8	32.5	25.4	41.6	<10.0	640.0
			POST	122	121	99.2	95.5	100	330.1	262.7	414.9	<10.0	7241.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 57 **Seroconversion rate (SCR) for HI antibody titers post last vaccination by previous influenza vaccination status for subjects aged between 3 to 8 years old (Total vaccinated cohort)**

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	315	285	90.5	86.7	93.5
		prim	118	98	83.1	75.0	89.3
	TIV-VB	Unprm	318	298	93.7	90.5	96.1
		prim	117	104	88.9	81.7	93.9
	TIV-YB	Unprm	315	290	92.1	88.5	94.8
		prim	122	101	82.8	74.9	89.0
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	315	223	70.8	65.4	75.8
		prim	118	76	64.4	55.1	73.0
	TIV-VB	Unprm	318	228	71.7	66.4	76.6
		prim	117	64	54.7	45.2	63.9
	TIV-YB	Unprm	313	232	74.1	68.9	78.9
		prim	122	68	55.7	46.5	64.7
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	315	258	81.9	77.2	86.0
		prim	118	80	67.8	58.6	76.1
	TIV-VB	Unprm	318	260	81.8	77.1	85.8
		prim	117	78	66.7	57.4	75.1
	TIV-YB	Unprm	313	97	31.0	25.9	36.4
		prim	122	39	32.0	23.8	41.0
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	315	277	87.9	83.8	91.3
		prim	118	99	83.9	76.0	90.0
	TIV-VB	Unprm	318	137	43.1	37.6	48.7
		prim	117	53	45.3	36.1	54.8
	TIV-YB	Unprm	315	282	89.5	85.6	92.7
		prim	122	102	83.6	75.8	89.7

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 58 **Seroprotection rates for HI antibody titers by previous influenza vaccination status for subjects aged between 3 to 8 years old (Total vaccinated cohort)**

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
A/California/7/2009 (H1N1)	QIV1	Unprm	PRE	346	169	48.8	43.5	54.2
			POST	317	304	95.9	93.1	97.8
		prim	PRE	119	63	52.9	43.6	62.2
			POST	118	111	94.1	88.2	97.6
	TIV-VB	Unprm	PRE	338	182	53.8	48.4	59.3
			POST	318	309	97.2	94.7	98.7
		prim	PRE	123	57	46.3	37.3	55.6
			POST	118	115	97.5	92.7	99.5
	TIV-YB	Unprm	PRE	335	169	50.4	45.0	55.9
			POST	315	303	96.2	93.4	98.0
		prim	PRE	127	51	40.2	31.6	49.2
			POST	122	114	93.4	87.5	97.1
A/Victoria/210/2009 (H3N2)	QIV1	Unprm	PRE	346	128	37.0	31.9	42.3
			POST	317	289	91.2	87.5	94.1
		prim	PRE	119	47	39.5	30.7	48.9
			POST	118	100	84.7	77.0	90.7
	TIV-VB	Unprm	PRE	338	138	40.8	35.5	46.3
			POST	318	299	94.0	90.8	96.4
		prim	PRE	123	49	39.8	31.1	49.1
			POST	118	103	87.3	79.9	92.7
	TIV-YB	Unprm	PRE	333	129	38.7	33.5	44.2
			POST	315	294	93.3	90.0	95.8
		prim	PRE	127	48	37.8	29.3	46.8
			POST	122	104	85.2	77.7	91.0
B/Brisbane/60/2008 (Victoria)	QIV1	Unprm	PRE	346	118	34.1	29.1	39.4
			POST	317	304	95.9	93.1	97.8
		prim	PRE	119	41	34.5	26.0	43.7
			POST	118	104	88.1	80.9	93.4
	TIV-VB	Unprm	PRE	338	129	38.2	33.0	43.6
			POST	318	311	97.8	95.5	99.1
		prim	PRE	123	47	38.2	29.6	47.4
			POST	118	107	90.7	83.9	95.3
	TIV-YB	Unprm	PRE	334	117	35.0	29.9	40.4
			POST	314	195	62.1	56.5	67.5
		prim	PRE	127	44	34.6	26.4	43.6
			POST	122	85	69.7	60.7	77.7
B/Florida/4/2006 (Yamagata)	QIV1	Unprm	PRE	346	168	48.6	43.2	54.0
			POST	317	316	99.7	98.3	100
		prim	PRE	119	59	49.6	40.3	58.9
			POST	118	113	95.8	90.4	98.6
	TIV-VB	Unprm	PRE	338	157	46.4	41.0	51.9
			POST	318	265	83.3	78.8	87.3
		prim	PRE	123	67	54.5	45.2	63.5
			POST	118	107	90.7	83.9	95.3
	TIV-YB	Unprm	PRE	335	166	49.6	44.1	55.0
			POST	315	313	99.4	97.7	99.9
		prim	PRE	127	70	55.1	46.0	63.9
			POST	122	119	97.5	93.0	99.5

QIV1 = Flu Q-QIV (3 - 17 years)

TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titer ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Day 0
POST=Day 28 post last vaccination

Supplement 59 Seroconversion Factor (SCF) for HI antibody titers post last vaccination by previous influenza vaccination status for subjects aged between 3 to 8 years old (Total vaccinated cohort)

				SCF		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1) (1/DIL)	QIV1	Unprm	315	13.86	12.40	15.48
		prim	118	9.43	7.71	11.53
	TIV-VB	Unprm	318	15.22	13.59	17.04
		prim	117	12.16	9.82	15.04
	TIV-YB	Unprm	315	15.93	14.31	17.74
		prim	122	11.65	9.53	14.24
A/Victoria/210/2009 (H3N2) (1/DIL)	QIV1	Unprm	315	7.50	6.60	8.52
		prim	118	6.03	4.93	7.38
	TIV-VB	Unprm	318	7.48	6.60	8.47
		prim	117	5.57	4.39	7.08
	TIV-YB	Unprm	313	7.98	7.02	9.06
		prim	122	5.34	4.30	6.65
B/Brisbane/60/2008 (Victoria) (1/DIL)	QIV1	Unprm	315	12.46	10.83	14.33
		prim	118	7.37	5.88	9.24
	TIV-VB	Unprm	318	11.49	9.99	13.22
		prim	117	6.60	5.25	8.30
	TIV-YB	Unprm	313	2.84	2.51	3.20
		prim	122	2.89	2.44	3.43
B/Florida/4/2006 (Yamagata) (1/DIL)	QIV1	Unprm	315	14.34	12.47	16.48
		prim	118	10.49	8.45	13.03
	TIV-VB	Unprm	318	3.52	3.15	3.92
		prim	117	3.61	3.00	4.34
	TIV-YB	Unprm	315	15.90	13.86	18.24
		prim	122	9.91	8.21	11.95

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
Unprm = Unprimed subjects
prim = primed subjects
N = Number of subjects with pre- and post-vaccination results available
SCF = Fold increase in serum HI GMTs post-vaccination
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 60 Incidence and nature of symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	QIV1	932	657	70.5	67.5	73.4	932	337	36.2	33.1	39.3	932	601	64.5	61.3	67.6
	TIV-VB	929	578	62.2	59.0	65.3	929	334	36.0	32.9	39.1	929	506	54.5	51.2	57.7
	TIV-YB	932	578	62.0	58.8	65.1	932	328	35.2	32.1	38.4	932	515	55.3	52.0	58.5
	QIV2	301	193	64.1	58.4	69.5	301	144	47.8	42.1	53.6	301	137	45.5	39.8	51.3
Dose 2	QIV1	331	184	55.6	50.1	61.0	331	76	23.0	18.5	27.9	331	171	51.7	46.1	57.2
	TIV-VB	330	173	52.4	46.9	57.9	330	71	21.5	17.2	26.3	330	155	47.0	41.5	52.5
	TIV-YB	328	160	48.8	43.3	54.3	328	64	19.5	15.4	24.2	328	145	44.2	38.8	49.8
	QIV2	233	122	52.4	45.7	58.9	233	86	36.9	30.7	43.5	233	85	36.5	30.3	43.0
Overall/dose	QIV1	1263	841	66.6	63.9	69.2	1263	413	32.7	30.1	35.4	1263	772	61.1	58.4	63.8
	TIV-VB	1259	751	59.7	56.9	62.4	1259	405	32.2	29.6	34.8	1259	661	52.5	49.7	55.3
	TIV-YB	1260	738	58.6	55.8	61.3	1260	392	31.1	28.6	33.7	1260	660	52.4	49.6	55.2
	QIV2	534	315	59.0	54.7	63.2	534	230	43.1	38.8	47.4	534	222	41.6	37.4	45.9
Overall/subject	QIV1	932	691	74.1	71.2	76.9	932	364	39.1	35.9	42.3	932	642	68.9	65.8	71.8
	TIV-VB	929	620	66.7	63.6	69.8	929	365	39.3	36.1	42.5	929	550	59.2	56.0	62.4
	TIV-YB	932	606	65.0	61.9	68.1	932	350	37.6	34.4	40.8	932	546	58.6	55.3	61.8
	QIV2	301	212	70.4	64.9	75.5	301	169	56.1	50.3	61.8	301	156	51.8	46.0	57.6

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 61 Incidence and nature of grade 3 symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	QIV1	932	46	4.9	3.6	6.5	932	20	2.1	1.3	3.3	932	31	3.3	2.3	4.7
	TIV-VB	929	36	3.9	2.7	5.3	929	22	2.4	1.5	3.6	929	16	1.7	1.0	2.8
	TIV-YB	932	37	4.0	2.8	5.4	932	21	2.3	1.4	3.4	932	22	2.4	1.5	3.6
	QIV2	301	18	6.0	3.6	9.3	301	15	5.0	2.8	8.1	301	3	1.0	0.2	2.9
Dose 2	QIV1	331	10	3.0	1.5	5.5	331	5	1.5	0.5	3.5	331	6	1.8	0.7	3.9
	TIV-VB	330	12	3.6	1.9	6.3	330	8	2.4	1.1	4.7	330	5	1.5	0.5	3.5
	TIV-YB	328	9	2.7	1.3	5.1	328	4	1.2	0.3	3.1	328	6	1.8	0.7	3.9
	QIV2	233	11	4.7	2.4	8.3	233	7	3.0	1.2	6.1	233	6	2.6	1.0	5.5
Overall/dose	QIV1	1263	56	4.4	3.4	5.7	1263	25	2.0	1.3	2.9	1263	37	2.9	2.1	4.0
	TIV-VB	1259	48	3.8	2.8	5.0	1259	30	2.4	1.6	3.4	1259	21	1.7	1.0	2.5
	TIV-YB	1260	46	3.7	2.7	4.8	1260	25	2.0	1.3	2.9	1260	28	2.2	1.5	3.2
	QIV2	534	29	5.4	3.7	7.7	534	22	4.1	2.6	6.2	534	9	1.7	0.8	3.2
Overall/subject	QIV1	932	55	5.9	4.5	7.6	932	25	2.7	1.7	3.9	932	37	4.0	2.8	5.4
	TIV-VB	929	46	5.0	3.6	6.5	929	28	3.0	2.0	4.3	929	21	2.3	1.4	3.4
	TIV-YB	932	43	4.6	3.4	6.2	932	25	2.7	1.7	3.9	932	26	2.8	1.8	4.1
	QIV2	301	25	8.3	5.4	12.0	301	20	6.6	4.1	10.1	301	8	2.7	1.2	5.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Supplement 62 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (3-8y/9-17y) (Total vaccinated cohort)

		QIV1										TIV-VB				
		3-8y					9-17y					3-8y				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	N	%	LL	UL
Dose 1																
Pain	All	456	273	59.9	55.2	64.4	457	324	70.9	66.5	75.0	452	220	48.7	44.0	53.4
	Grade 2*3	456	77	16.9	13.6	20.6	457	112	24.5	20.6	28.7	452	52	11.5	8.7	14.8
	Grade 3	456	9	2.0	0.9	3.7	457	20	4.4	2.7	6.7	452	9	2.0	0.9	3.7
	Med adv	456	0	0.0	0.0	0.8	457	0	0.0	0.0	0.8	452	0	0.0	0.0	0.8
Redness (mm)	All	456	29	6.4	4.3	9.0	457	19	4.2	2.5	6.4	452	14	3.1	1.7	5.1
	[50 - ...	456	16	3.5	2.0	5.6	457	8	1.8	0.8	3.4	452	4	0.9	0.2	2.3
	>100	456	0	0.0	0.0	0.8	457	1	0.2	0.0	1.2	452	0	0.0	0.0	0.8
	Med adv	456	2	0.4	0.1	1.6	457	2	0.4	0.1	1.6	452	1	0.2	0.0	1.2
Swelling (mm)	All	456	28	6.1	4.1	8.8	457	29	6.3	4.3	9.0	452	16	3.5	2.0	5.7
	[50 - ...	456	10	2.2	1.1	4.0	457	13	2.8	1.5	4.8	452	2	0.4	0.1	1.6
	>100	456	0	0.0	0.0	0.8	457	1	0.2	0.0	1.2	452	0	0.0	0.0	0.8
	Med adv	456	1	0.2	0.0	1.2	457	1	0.2	0.0	1.2	452	0	0.0	0.0	0.8
Dose 2																
Pain	All	324	169	52.2	46.6	57.7						322	151	46.9	41.3	52.5
	Grade 2*3	324	48	14.8	11.1	19.2						322	34	10.6	7.4	14.4
	Grade 3	324	6	1.9	0.7	4.0						322	5	1.6	0.5	3.6
	Med adv	324	0	0.0	0.0	1.1						322	0	0.0	0.0	1.1
Redness (mm)	All	324	13	4.0	2.2	6.8						322	11	3.4	1.7	6.0
	[50 - ...	324	6	1.9	0.7	4.0						322	5	1.6	0.5	3.6
	>100	324	0	0.0	0.0	1.1						322	0	0.0	0.0	1.1
	Med adv	324	0	0.0	0.0	1.1						322	0	0.0	0.0	1.1
Swelling (mm)	All	324	12	3.7	1.9	6.4						322	15	4.7	2.6	7.6
	[50 - ...	324	6	1.9	0.7	4.0						322	3	0.9	0.2	2.7
	>100	324	0	0.0	0.0	1.1						322	0	0.0	0.0	1.1
	Med adv	324	0	0.0	0.0	1.1						322	0	0.0	0.0	1.1
Overall/dose																
Pain	All	780	442	56.7	53.1	60.2	457	324	70.9	66.5	75.0	774	371	47.9	44.4	51.5
	Grade 2*3	780	125	16.0	13.5	18.8	457	112	24.5	20.6	28.7	774	86	11.1	9.0	13.5
	Grade 3	780	15	1.9	1.1	3.2	457	20	4.4	2.7	6.7	774	14	1.8	1.0	3.0
	Med adv	780	0	0.0	0.0	0.5	457	0	0.0	0.0	0.8	774	0	0.0	0.0	0.5
Redness (mm)	All	780	42	5.4	3.9	7.2	457	19	4.2	2.5	6.4	774	25	3.2	2.1	4.7
	[50 - ...	780	22	2.8	1.8	4.2	457	8	1.8	0.8	3.4	774	9	1.2	0.5	2.2
	>100	780	0	0.0	0.0	0.5	457	1	0.2	0.0	1.2	774	0	0.0	0.0	0.5
	Med adv	780	2	0.3	0.0	0.9	457	2	0.4	0.1	1.6	774	1	0.1	0.0	0.7
Swelling (mm)	All	780	40	5.1	3.7	6.9	457	29	6.3	4.3	9.0	774	31	4.0	2.7	5.6
	[50 - ...	780	16	2.1	1.2	3.3	457	13	2.8	1.5	4.8	774	5	0.6	0.2	1.5
	>100	780	0	0.0	0.0	0.5	457	1	0.2	0.0	1.2	774	0	0.0	0.0	0.5
	Med adv	780	1	0.1	0.0	0.7	457	1	0.2	0.0	1.2	774	0	0.0	0.0	0.5
Overall/subject																
Pain	All	456	313	68.6	64.2	72.9	457	324	70.9	66.5	75.0	453	261	57.6	52.9	62.2
	Grade 2*3	456	104	22.8	19.0	26.9	457	112	24.5	20.6	28.7	453	76	16.8	13.5	20.5
	Grade 3	456	15	3.3	1.9	5.4	457	20	4.4	2.7	6.7	453	14	3.1	1.7	5.1
	Med adv	456	0	0.0	0.0	0.8	457	0	0.0	0.0	0.8	453	0	0.0	0.0	0.8
Redness (mm)	All	456	38	8.3	6.0	11.3	457	19	4.2	2.5	6.4	453	23	5.1	3.2	7.5
	[50 - ...	456	20	4.4	2.7	6.7	457	8	1.8	0.8	3.4	453	8	1.8	0.8	3.4
	>100	456	0	0.0	0.0	0.8	457	1	0.2	0.0	1.2	453	0	0.0	0.0	0.8

		QIV1										TIV-VB				
		3-8y					9-17y					3-8y				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**N**	**%**	**LL**	**UL**
	Med adv	456	2	0.4	0.1	1.6	457	2	0.4	0.1	1.6	453	1	0.2	0.0	1.2
Swelling (mm)	All	456	35	7.7	5.4	10.5	457	29	6.3	4.3	9.0	453	26	5.7	3.8	8.3
	[50 - ...	456	13	2.9	1.5	4.8	457	13	2.8	1.5	4.8	453	5	1.1	0.4	2.6
	>100	456	0	0.0	0.0	0.8	457	1	0.2	0.0	1.2	453	0	0.0	0.0	0.8
	Med adv	456	1	0.2	0.0	1.2	457	1	0.2	0.0	1.2	453	0	0.0	0.0	0.8

		TIV-VB					TIV-YB									
		9-17y					3-8y					9-17y				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**N**	**%**	**LL**	**UL**
Dose 1																
Pain	All	458	277	60.5	55.8	65.0	454	233	51.3	46.6	56.0	461	277	60.1	55.5	64.6
	Grade 2*3	458	66	14.4	11.3	18.0	454	62	13.7	10.6	17.2	461	68	14.8	11.6	18.3
	Grade 3	458	7	1.5	0.6	3.1	454	11	2.4	1.2	4.3	461	11	2.4	1.2	4.2
	Med adv	458	0	0.0	0.0	0.8	454	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
Redness (mm)	All	458	15	3.3	1.8	5.3	454	19	4.2	2.5	6.5	461	13	2.8	1.5	4.8
	[50 - ...	458	2	0.4	0.1	1.6	454	6	1.3	0.5	2.9	461	2	0.4	0.1	1.6
	>100	458	0	0.0	0.0	0.8	454	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
	Med adv	458	0	0.0	0.0	0.8	454	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
Swelling (mm)	All	458	14	3.1	1.7	5.1	454	14	3.1	1.7	5.1	461	21	4.6	2.8	6.9
	[50 - ...	458	1	0.2	0.0	1.2	454	6	1.3	0.5	2.9	461	6	1.3	0.5	2.8
	>100	458	0	0.0	0.0	0.8	454	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
	Med adv	458	0	0.0	0.0	0.8	454	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
Dose 2																
Pain	All						317	140	44.2	38.6	49.8	1	1	100	2.5	100
	Grade 2*3						317	32	10.1	7.0	14.0	1	1	100	2.5	100
	Grade 3						317	6	1.9	0.7	4.1	1	0	0.0	0.0	97.5
	Med adv						317	0	0.0	0.0	1.2	1	0	0.0	0.0	97.5
Redness (mm)	All						317	10	3.2	1.5	5.7	1	0	0.0	0.0	97.5
	[50 - ...						317	4	1.3	0.3	3.2	1	0	0.0	0.0	97.5
	>100						317	0	0.0	0.0	1.2	1	0	0.0	0.0	97.5
	Med adv						317	0	0.0	0.0	1.2	1	0	0.0	0.0	97.5
Swelling (mm)	All						317	7	2.2	0.9	4.5	1	0	0.0	0.0	97.5
	[50 - ...						317	2	0.6	0.1	2.3	1	0	0.0	0.0	97.5
	>100						317	0	0.0	0.0	1.2	1	0	0.0	0.0	97.5
	Med adv						317	0	0.0	0.0	1.2	1	0	0.0	0.0	97.5
Overall/dose																
Pain	All	458	277	60.5	55.8	65.0	771	373	48.4	44.8	52.0	462	278	60.2	55.5	64.7
	Grade 2*3	458	66	14.4	11.3	18.0	771	94	12.2	10.0	14.7	462	69	14.9	11.8	18.5
	Grade 3	458	7	1.5	0.6	3.1	771	17	2.2	1.3	3.5	462	11	2.4	1.2	4.2
	Med adv	458	0	0.0	0.0	0.8	771	0	0.0	0.0	0.5	462	0	0.0	0.0	0.8
Redness (mm)	All	458	15	3.3	1.8	5.3	771	29	3.8	2.5	5.4	462	13	2.8	1.5	4.8
	[50 - ...	458	2	0.4	0.1	1.6	771	10	1.3	0.6	2.4	462	2	0.4	0.1	1.6
	>100	458	0	0.0	0.0	0.8	771	0	0.0	0.0	0.5	462	0	0.0	0.0	0.8
	Med adv	458	0	0.0	0.0	0.8	771	0	0.0	0.0	0.5	462	0	0.0	0.0	0.8
Swelling (mm)	All	458	14	3.1	1.7	5.1	771	21	2.7	1.7	4.1	462	21	4.5	2.8	6.9
	[50 - ...	458	1	0.2	0.0	1.2	771	8	1.0	0.4	2.0	462	6	1.3	0.5	2.8
	>100	458	0	0.0	0.0	0.8	771	0	0.0	0.0	0.5	462	0	0.0	0.0	0.8
	Med adv	458	0	0.0	0.0	0.8	771	0	0.0	0.0	0.5	462	0	0.0	0.0	0.8
Overall/subject																
Pain	All	458	277	60.5	55.8	65.0	455	265	58.2	53.6	62.8	461	277	60.1	55.5	64.6
	Grade 2*3	458	66	14.4	11.3	18.0	455	80	17.6	14.2	21.4	461	69	15.0	11.8	18.6

		TIV-VB					TIV-YB									
		9-17y					3-8y					9-17y				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3	458	7	1.5	0.6	3.1	455	15	3.3	1.9	5.4	461	11	2.4	1.2	4.2
	Med adv	458	0	0.0	0.0	0.8	455	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
Redness (mm)	All	458	15	3.3	1.8	5.3	455	23	5.1	3.2	7.5	461	13	2.8	1.5	4.8
	[50 - ...	458	2	0.4	0.1	1.6	455	7	1.5	0.6	3.1	461	2	0.4	0.1	1.6
	>100	458	0	0.0	0.0	0.8	455	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
	Med adv	458	0	0.0	0.0	0.8	455	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
Swelling (mm)	All	458	14	3.1	1.7	5.1	455	18	4.0	2.4	6.2	461	21	4.6	2.8	6.9
	[50 - ...	458	1	0.2	0.0	1.2	455	6	1.3	0.5	2.8	461	6	1.3	0.5	2.8
	>100	458	0	0.0	0.0	0.8	455	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8
	Med adv	458	0	0.0	0.0	0.8	455	0	0.0	0.0	0.8	461	0	0.0	0.0	0.8

		Total									
		3-8y					9-17y				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1											
Pain	All	1362	726	53.3	50.6	56.0	1376	878	63.8	61.2	66.4
	Grade 2*3	1362	191	14.0	12.2	16.0	1376	246	17.9	15.9	20.0
	Grade 3	1362	29	2.1	1.4	3.0	1376	38	2.8	2.0	3.8
	Med adv	1362	0	0.0	0.0	0.3	1376	0	0.0	0.0	0.3
Redness (mm)	All	1362	62	4.6	3.5	5.8	1376	47	3.4	2.5	4.5
	[50 - ...	1362	26	1.9	1.3	2.8	1376	12	0.9	0.5	1.5
	>100	1362	0	0.0	0.0	0.3	1376	1	0.1	0.0	0.4
	Med adv	1362	3	0.2	0.0	0.6	1376	2	0.1	0.0	0.5
Swelling (mm)	All	1362	58	4.3	3.2	5.5	1376	64	4.7	3.6	5.9
	[50 - ...	1362	18	1.3	0.8	2.1	1376	20	1.5	0.9	2.2
	>100	1362	0	0.0	0.0	0.3	1376	1	0.1	0.0	0.4
	Med adv	1362	1	0.1	0.0	0.4	1376	1	0.1	0.0	0.4
Dose 2											
Pain	All	963	460	47.8	44.6	51.0	1	1	100	2.5	100
	Grade 2*3	963	114	11.8	9.9	14.0	1	1	100	2.5	100
	Grade 3	963	17	1.8	1.0	2.8	1	0	0.0	0.0	97.5
	Med adv	963	0	0.0	0.0	0.4	1	0	0.0	0.0	97.5
Redness (mm)	All	963	34	3.5	2.5	4.9	1	0	0.0	0.0	97.5
	[50 - ...	963	15	1.6	0.9	2.6	1	0	0.0	0.0	97.5
	>100	963	0	0.0	0.0	0.4	1	0	0.0	0.0	97.5
	Med adv	963	0	0.0	0.0	0.4	1	0	0.0	0.0	97.5
Swelling (mm)	All	963	34	3.5	2.5	4.9	1	0	0.0	0.0	97.5
	[50 - ...	963	11	1.1	0.6	2.0	1	0	0.0	0.0	97.5
	>100	963	0	0.0	0.0	0.4	1	0	0.0	0.0	97.5
	Med adv	963	0	0.0	0.0	0.4	1	0	0.0	0.0	97.5
Overall/dose											
Pain	All	2325	1186	51.0	49.0	53.1	1377	879	63.8	61.2	66.4
	Grade 2*3	2325	305	13.1	11.8	14.6	1377	247	17.9	15.9	20.1
	Grade 3	2325	46	2.0	1.5	2.6	1377	38	2.8	2.0	3.8
	Med adv	2325	0	0.0	0.0	0.2	1377	0	0.0	0.0	0.3
Redness (mm)	All	2325	96	4.1	3.4	5.0	1377	47	3.4	2.5	4.5
	[50 - ...	2325	41	1.8	1.3	2.4	1377	12	0.9	0.5	1.5
	>100	2325	0	0.0	0.0	0.2	1377	1	0.1	0.0	0.4
	Med adv	2325	3	0.1	0.0	0.4	1377	2	0.1	0.0	0.5
Swelling (mm)	All	2325	92	4.0	3.2	4.8	1377	64	4.6	3.6	5.9
	[50 - ...	2325	29	1.2	0.8	1.8	1377	20	1.5	0.9	2.2

		Total									
		3-8y					9-17y				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	>100	2325	0	0.0	0.0	0.2	1377	1	0.1	0.0	0.4
	Med adv	2325	1	0.0	0.0	0.2	1377	1	0.1	0.0	0.4
Overall/subject											
Pain	All	1364	839	61.5	58.9	64.1	1376	878	63.8	61.2	66.4
	Grade 2*3	1364	260	19.1	17.0	21.2	1376	247	18.0	16.0	20.1
	Grade 3	1364	44	3.2	2.4	4.3	1376	38	2.8	2.0	3.8
	Med adv	1364	0	0.0	0.0	0.3	1376	0	0.0	0.0	0.3
Redness (mm)	All	1364	84	6.2	4.9	7.6	1376	47	3.4	2.5	4.5
	[50 - ...	1364	35	2.6	1.8	3.6	1376	12	0.9	0.5	1.5
	>100	1364	0	0.0	0.0	0.3	1376	1	0.1	0.0	0.4
	Med adv	1364	3	0.2	0.0	0.6	1376	2	0.1	0.0	0.5
Swelling (mm)	All	1364	79	5.8	4.6	7.2	1376	64	4.7	3.6	5.9
	[50 - ...	1364	24	1.8	1.1	2.6	1376	20	1.5	0.9	2.2
	>100	1364	0	0.0	0.0	0.3	1376	1	0.1	0.0	0.4
	Med adv	1364	1	0.1	0.0	0.4	1376	1	0.1	0.0	0.4

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
3-8y = Subjects aged between 3 years to 8 years
9-17y = Subjects aged between 9 years to 17 years
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
Total : n/%= number/percentage of subjects/doses with at least one local symptom whatever the number of injections.
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Supplement 63 Number of days with local symptoms during the 7-day post-vaccination period (Total vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max
Pain	Dose 1	QIV1	597	2.2	1.0	1.0	2.0	3.0	7.0
		TIV-VB	497	2.1	1.0	1.0	2.0	3.0	7.0
		TIV-YB	510	2.0	1.0	1.0	2.0	3.0	7.0
		QIV2	131	1.8	1.0	1.0	1.0	2.0	7.0
	Dose 2	QIV1	169	1.9	1.0	1.0	2.0	2.0	7.0
		TIV-VB	151	1.8	1.0	1.0	2.0	2.0	7.0
		TIV-YB	141	1.8	1.0	1.0	2.0	2.0	7.0
		QIV2	76	2.0	1.0	1.0	2.0	2.0	7.0
	Overall/dose	QIV1	766	2.1	1.0	1.0	2.0	3.0	7.0
		TIV-VB	648	2.0	1.0	1.0	2.0	2.0	7.0
		TIV-YB	651	2.0	1.0	1.0	2.0	2.0	7.0
		QIV2	207	1.9	1.0	1.0	1.0	2.0	7.0
Redness	Dose 1	QIV1	48	2.4	1.0	1.0	2.0	3.0	7.0
		TIV-VB	29	1.8	1.0	1.0	1.0	2.0	6.0
		TIV-YB	32	1.9	1.0	1.0	1.0	2.0	7.0
		QIV2	13	2.8	1.0	1.0	1.0	5.0	7.0
	Dose 2	QIV1	13	2.0	1.0	1.0	2.0	3.0	3.0
		TIV-VB	11	2.0	1.0	1.0	1.0	3.0	6.0
		TIV-YB	10	2.3	1.0	1.0	1.5	3.0	6.0
		QIV2	14	2.9	1.0	1.0	2.5	4.0	6.0
	Overall/dose	QIV1	61	2.3	1.0	1.0	2.0	3.0	7.0
		TIV-VB	40	1.9	1.0	1.0	1.0	2.0	6.0
		TIV-YB	42	2.0	1.0	1.0	1.0	2.0	7.0
		QIV2	27	2.9	1.0	1.0	2.0	5.0	7.0
Swelling	Dose 1	QIV1	57	2.2	1.0	1.0	2.0	2.0	7.0
		TIV-VB	30	2.1	1.0	1.0	2.0	2.0	7.0
		TIV-YB	35	1.9	1.0	1.0	2.0	2.0	7.0
		QIV2	10	2.3	1.0	1.0	1.5	3.0	5.0
	Dose 2	QIV1	12	2.9	1.0	2.0	2.5	4.0	6.0
		TIV-VB	15	1.9	1.0	1.0	2.0	2.0	4.0
		TIV-YB	7	1.9	1.0	1.0	2.0	2.0	4.0
		QIV2	11	3.0	1.0	2.0	3.0	4.0	5.0
	Overall/dose	QIV1	69	2.3	1.0	1.0	2.0	3.0	7.0
		TIV-VB	45	2.0	1.0	1.0	2.0	2.0	7.0
		TIV-YB	42	1.9	1.0	1.0	2.0	2.0	7.0
		QIV2	21	2.7	1.0	1.0	2.0	4.0	5.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victotria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
N = Number of subjects with the symptom and without the missing confirmed grade
Q1 = 25th percentile
Q3 = 75th percentile

Supplement 64 Number of days with general symptoms during the 7-day post-vaccination period (Total vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max
Drowsiness	Dose 1	QIV1	39	1.6	1.0	1.0	1.0	2.0	4.0
		TIV-VB	37	2.0	1.0	1.0	2.0	2.0	7.0
		TIV-YB	44	1.8	1.0	1.0	1.0	2.0	7.0
		QIV2	85	2.2	1.0	1.0	2.0	3.0	7.0
	Dose 2	QIV1	16	1.4	1.0	1.0	1.0	1.5	3.0
		TIV-VB	18	1.9	1.0	1.0	1.0	2.0	7.0
		TIV-YB	17	2.2	1.0	1.0	2.0	3.0	7.0
		QIV2	45	2.4	1.0	1.0	2.0	3.0	7.0
	Overall/dose	QIV1	55	1.5	1.0	1.0	1.0	2.0	4.0
		TIV-VB	55	1.9	1.0	1.0	1.0	2.0	7.0
		TIV-YB	61	1.9	1.0	1.0	1.0	2.0	7.0
		QIV2	130	2.2	1.0	1.0	2.0	3.0	7.0
Fatigue	Dose 1	QIV1	161	2.4	1.0	1.0	2.0	3.0	7.0
		TIV-VB	171	2.0	1.0	1.0	1.0	3.0	7.0
		TIV-YB	167	2.2	1.0	1.0	2.0	3.0	7.0
	Dose 2	QIV1	27	2.0	1.0	1.0	2.0	3.0	6.0
		TIV-VB	19	2.1	1.0	1.0	2.0	3.0	6.0
		TIV-YB	19	2.5	1.0	1.0	2.0	3.0	7.0
	Overall/dose	QIV1	188	2.3	1.0	1.0	2.0	3.0	7.0
		TIV-VB	190	2.0	1.0	1.0	1.0	3.0	7.0
		TIV-YB	186	2.2	1.0	1.0	2.0	3.0	7.0
Gastrointestinal	Dose 1	QIV1	70	2.3	1.0	1.0	1.5	3.0	7.0
		TIV-VB	70	2.0	1.0	1.0	1.0	3.0	7.0
		TIV-YB	65	1.8	1.0	1.0	1.0	2.0	7.0
	Dose 2	QIV1	17	1.6	1.0	1.0	1.0	2.0	4.0
		TIV-VB	16	1.8	1.0	1.0	1.5	2.0	7.0
		TIV-YB	9	2.0	1.0	1.0	2.0	2.0	5.0
	Overall/dose	QIV1	87	2.1	1.0	1.0	1.0	3.0	7.0
		TIV-VB	86	1.9	1.0	1.0	1.0	2.0	7.0
		TIV-YB	74	1.8	1.0	1.0	1.0	2.0	7.0
Headache	Dose 1	QIV1	160	2.1	1.0	1.0	2.0	2.0	7.0
		TIV-VB	160	1.9	1.0	1.0	1.0	2.0	7.0
		TIV-YB	146	2.1	1.0	1.0	2.0	3.0	7.0
	Dose 2	QIV1	20	1.8	1.0	1.0	1.5	2.5	4.0
		TIV-VB	19	1.6	1.0	1.0	1.0	2.0	4.0
		TIV-YB	17	1.8	1.0	1.0	1.0	2.0	7.0
	Overall/dose	QIV1	180	2.1	1.0	1.0	2.0	2.0	7.0
		TIV-VB	179	1.8	1.0	1.0	1.0	2.0	7.0
		TIV-YB	163	2.1	1.0	1.0	2.0	3.0	7.0
Irritability	Dose 1	QIV1	48	1.5	1.0	1.0	1.0	2.0	7.0
		TIV-VB	31	2.3	1.0	1.0	2.0	4.0	7.0
		TIV-YB	41	2.2	1.0	1.0	2.0	3.0	7.0
		QIV2	120	2.5	1.0	1.0	2.0	3.0	7.0
	Dose 2	QIV1	25	2.0	1.0	1.0	1.0	2.0	6.0
		TIV-VB	22	2.3	1.0	1.0	2.0	3.0	7.0
		TIV-YB	16	2.6	1.0	1.0	2.0	3.5	7.0
		QIV2	74	2.6	1.0	1.0	2.0	3.0	7.0
	Overall/dose	QIV1	73	1.7	1.0	1.0	1.0	2.0	7.0
		TIV-VB	53	2.3	1.0	1.0	2.0	3.0	7.0
		TIV-YB	57	2.3	1.0	1.0	2.0	3.0	7.0
		QIV2	194	2.5	1.0	1.0	2.0	3.0	7.0

Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max
Joint pain at other location	Dose 1	QIV1	94	2.1	1.0	1.0	2.0	2.0	7.0
		TIV-VB	86	2.1	1.0	1.0	2.0	3.0	7.0
		TIV-YB	76	2.2	1.0	1.0	1.5	3.0	7.0
	Dose 2	QIV1	21	2.1	1.0	1.0	2.0	2.0	7.0
		TIV-VB	13	1.5	1.0	1.0	1.0	2.0	5.0
		TIV-YB	10	1.4	1.0	1.0	1.0	2.0	3.0
	Overall/dose	QIV1	115	2.1	1.0	1.0	2.0	2.0	7.0
		TIV-VB	99	2.0	1.0	1.0	2.0	3.0	7.0
		TIV-YB	86	2.1	1.0	1.0	1.0	3.0	7.0
Loss of appetite	Dose 1	QIV1	32	1.8	1.0	1.0	1.0	2.0	6.0
		TIV-VB	30	2.3	1.0	1.0	2.0	3.0	7.0
		TIV-YB	25	1.6	1.0	1.0	1.0	2.0	4.0
		QIV2	64	2.4	1.0	1.0	2.0	3.0	7.0
	Dose 2	QIV1	13	2.5	1.0	1.0	2.0	3.0	6.0
		TIV-VB	15	2.7	1.0	1.0	2.0	4.0	7.0
		TIV-YB	14	3.1	1.0	1.0	3.0	5.0	7.0
		QIV2	48	2.4	1.0	1.0	2.0	3.0	7.0
	Overall/dose	QIV1	45	2.0	1.0	1.0	1.0	2.0	6.0
		TIV-VB	45	2.4	1.0	1.0	2.0	3.0	7.0
		TIV-YB	39	2.2	1.0	1.0	2.0	3.0	7.0
		QIV2	112	2.4	1.0	1.0	2.0	3.0	7.0
Muscle aches	Dose 1	QIV1	207	2.3	1.0	1.0	2.0	3.0	7.0
		TIV-VB	180	2.0	1.0	1.0	2.0	3.0	7.0
		TIV-YB	179	2.2	1.0	1.0	2.0	3.0	7.0
	Dose 2	QIV1	44	1.8	1.0	1.0	1.0	2.0	4.0
		TIV-VB	27	1.5	1.0	1.0	1.0	2.0	4.0
		TIV-YB	30	1.7	1.0	1.0	2.0	2.0	4.0
	Overall/dose	QIV1	251	2.2	1.0	1.0	2.0	3.0	7.0
		TIV-VB	207	1.9	1.0	1.0	2.0	3.0	7.0
		TIV-YB	209	2.1	1.0	1.0	2.0	3.0	7.0
Shivering	Dose 1	QIV1	51	2.1	1.0	1.0	1.0	3.0	7.0
		TIV-VB	50	2.1	1.0	1.0	2.0	2.0	7.0
		TIV-YB	50	2.2	1.0	1.0	1.0	3.0	7.0
	Dose 2	QIV1	8	1.6	1.0	1.0	1.5	2.0	3.0
		TIV-VB	1	1.0	1.0	1.0	1.0	1.0	1.0
		TIV-YB	4	1.8	1.0	1.5	2.0	2.0	2.0
	Overall/dose	QIV1	59	2.0	1.0	1.0	1.0	2.0	7.0
		TIV-VB	51	2.0	1.0	1.0	2.0	2.0	7.0
		TIV-YB	54	2.1	1.0	1.0	1.0	3.0	7.0
Temperature	Dose 1	QIV1	25	1.4	1.0	1.0	1.0	1.0	5.0
		TIV-VB	43	1.6	1.0	1.0	1.0	2.0	6.0
		TIV-YB	26	1.8	1.0	1.0	1.5	2.0	5.0
		QIV2	16	1.8	1.0	1.0	1.0	2.0	6.0
	Dose 2	QIV1	17	2.2	1.0	1.0	2.0	3.0	6.0
		TIV-VB	7	1.6	1.0	1.0	1.0	2.0	3.0
		TIV-YB	9	1.6	1.0	1.0	1.0	2.0	4.0
		QIV2	12	2.1	1.0	1.0	1.5	2.5	6.0
	Overall/dose	QIV1	42	1.7	1.0	1.0	1.0	2.0	6.0
		TIV-VB	50	1.6	1.0	1.0	1.0	2.0	6.0
		TIV-YB	35	1.7	1.0	1.0	1.0	2.0	5.0
		QIV2	28	1.9	1.0	1.0	1.0	2.0	6.0

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victotria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)

QIV2 = Flu Q-QIV (6 - 35 months)
N = Number of subjects with the symptom and without the missing confirmed grade
Q1 = 25th percentile
Q3 = 75th percentile

Supplement 65 Global Summary of unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

	Group				
	QIV1	**TIV-VB**	**TIV-YB**	**QIV2**	**Total**
Number of subjects with at least one unsolicited symptom reported	44	47	44	43	178
Number of doses followed by at least one unsolicited symptom	47	51	48	49	195
Number of unsolicited symptoms classified by MedDRA Preferred Term*	62	68	60	65	255
Number of unsolicited symptoms reported	62	69	60	66	257

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once

Supplement 66 Global Summary of grade 3 unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

	Group				
	QIV1	**TIV-VB**	**TIV-YB**	**QIV2**	**Total**
Number of subjects with at least one unsolicited symptom reported	7	5	3	4	19
Number of doses followed by at least one unsolicited symptom	7	5	3	4	19
Number of unsolicited symptoms classified by MedDRA Preferred Term*	8	6	3	4	21
Number of unsolicited symptoms reported	8	6	3	4	21

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once

Supplement 67 **Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)**

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		40	4.3	3.1	5.8	41	4.4	3.2	5.9	35	3.8	2.6	5.2	24	8.0	5.2	11.6
Congenital, familial and genetic disorders (10010331)	Vitello-intestinal duct remnant (10066969)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Middle ear effusion (10062545)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Eye disorders (10015919)	Lacrimation increased (10023644)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Gastrointestinal disorders (10017947)	Abdominal pain upper (10000087)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Constipation (10010774)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Diarrhoea (10012735)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	3	0.3	0.1	0.9	1	0.3	0.0	1.8
	Enteritis (10014866)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Gastritis (10017853)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gastrooesophageal reflux disease (10017885)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nausea (10028813)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Toothache (10044055)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Vomiting (10047700)	2	0.2	0.0	0.8	4	0.4	0.1	1.1	3	0.3	0.1	0.9	3	1.0	0.2	2.9
General disorders and administration site conditions (10018065)	Fatigue (10016256)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Influenza like illness (10022004)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Injection site warmth (10022112)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pain (10033371)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Pyrexia (10037660)	2	0.2	0.0	0.8	2	0.2	0.0	0.8	2	0.2	0.0	0.8	3	1.0	0.2	2.9

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Hepatobiliary disorders (10019805)	Biliary dyskinesia (10056529)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Infections and infestations (10021881)	Abscess (10000269)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Acute tonsillitis (10001093)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Bronchitis (10006451)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Croup infectious (10011416)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	2	0.7	0.1	2.4
	Ear infection (10014011)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Enterobiasis (10014881)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Enterovirus infection (10014909)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gastroenteritis (10017888)	3	0.3	0.1	0.9	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gastroenteritis viral (10017918)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	3	1.0	0.2	2.9
	Hand-foot-and-mouth disease (10019113)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Laryngitis (10023874)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Lower respiratory tract infection (10024968)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nasopharyngitis (10028810)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Otitis externa (10033072)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Pertussis (10034738)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pharyngitis (10034835)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pharyngitis streptococcal (10034839)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Pharyngotonsillitis (10049140)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Pneumonia (10035664)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	2	0.2	0.0	0.8	2	0.7	0.1	2.4

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Respiratory syncytial virus infection (10061603)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Respiratory tract infection (10062352)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Scarlet fever (10039587)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Sinusitis (10040753)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Streptococcal infection (10061372)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tonsillitis (10044008)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Upper respiratory tract infection (10046306)	4	0.4	0.1	1.1	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Varicella (10046980)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Viral infection (10047461)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Injury, poisoning and procedural complications (10022117)	Concussion (10010254)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Face injury (10050392)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Facial bones fracture (10016042)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Forearm fracture (10016997)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Hand fracture (10019114)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Head injury (10019196)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Humerus fracture (10020462)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Laceration (10023572)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Limb injury (10061225)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Mouth injury (10049294)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Radius fracture (10037802)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tibia fracture (10043827)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Traumatic brain injury (10060690)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Upper limb fracture (10061394)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint range of motion decreased (10048706)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Grand mal convulsion (10018659)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Headache (10019211)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Migraine (10027599)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Psychomotor hyperactivity (10037211)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Somnolence (10041349)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Psychiatric disorders (10037175)	Abnormal behaviour (10061422)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Affective disorder (10001443)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Anxiety (10002855)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Depression (10012378)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eating disorder (10014062)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Emotional disorder (10014551)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Renal and urinary disorders (10038359)	Enuresis (10014928)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.3	0.0	1.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Bronchial hyperreactivity (10066091)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Cough (10011224)	3	0.3	0.1	0.9	3	0.3	0.1	0.9	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Oropharyngeal pain (10068319)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Rhinorrhoea (10039101)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Sneezing (10041232)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Surgical and medical procedures (10042613)	Tooth extraction (10062132)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
At least one symptom = at least one symptom reported (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Supplement 68 **Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)**

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		44	4.7	3.5	6.3	47	5.1	3.7	6.7	44	4.7	3.5	6.3	43	14.3	10.5	18.8
Blood and lymphatic system disorders (10005329)	Neutropenia (10029354)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Middle ear effusion (10062545)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Eye disorders (10015919)	Conjunctivitis (10010741)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Lacrimation increased (10023644)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Gastrointestinal disorders (10017947)	Abdominal pain (10000081)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Abdominal pain upper (10000087)	2	0.2	0.0	0.8	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Constipation (10010774)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Diarrhoea (10012735)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	3	1.0	0.2	2.9
	Flatulence (10016766)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Gastritis (10017853)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Nausea (10028813)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Vomiting (10047700)	3	0.3	0.1	0.9	3	0.3	0.1	0.9	3	0.3	0.1	0.9	5	1.7	0.5	3.8
General disorders and administration site conditions (10018065)	Axillary pain (10048750)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Chest pain (10008479)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Chills (10008531)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Fatigue (10016256)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Influenza like illness (10022004)	2	0.2	0.0	0.8	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site anaesthesia (10022046)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site haematoma (10022066)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	3	0.3	0.1	0.9	2	0.7	0.1	2.4
	Injection site induration (10022075)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site pruritus (10022093)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site rash (10022094)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Injection site reaction (10022095)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Injection site urticaria (10022107)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site vesicles (10022111)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site warmth (10022112)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Irritability (10022998)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pain (10033371)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pyrexia (10037660)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Infections and infestations (10021881)	Gastroenteritis viral (10017918)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Lower respiratory tract infection (10024968)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Nasopharyngitis (10028810)	3	0.3	0.1	0.9	2	0.2	0.0	0.8	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Pharyngitis (10034835)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Pharyngitis streptococcal (10034839)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pneumonia (10035664)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Upper respiratory tract infection (10046306)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	0.4	6	2.0	0.7	4.3
	Viral infection (10047461)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Injury, poisoning and procedural complications (10022117)	Contusion (10050584)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint range of motion decreased (10048706)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Musculoskeletal pain (10028391)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Musculoskeletal stiffness (10052904)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Myalgia (10028411)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Neck pain (10028836)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Nervous system disorders (10029205)	Dizziness (10013573)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Febrile convulsion (10016284)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Grand mal convulsion (10018659)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Headache (10019211)	2	0.2	0.0	0.8	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Lethargy (10024264)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Presyncope (10036653)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Psychomotor hyperactivity (10037211)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Cough (10011224)	8	0.9	0.4	1.7	9	1.0	0.4	1.8	10	1.1	0.5	2.0	5	1.7	0.5	3.8
	Nasal congestion (10028735)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	3	0.3	0.1	0.9	2	0.7	0.1	2.4
	Oropharyngeal pain (10068319)	5	0.5	0.2	1.2	5	0.5	0.2	1.3	6	0.6	0.2	1.4	0	0.0	0.0	1.2
	Productive cough (10036790)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Respiratory tract congestion (10052251)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Rhinorrhoea (10039101)	4	0.4	0.1	1.1	4	0.4	0.1	1.1	6	0.6	0.2	1.4	13	4.3	2.3	7.3
	Sinus congestion (10040742)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Sneezing (10041232)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Wheezing (10047924)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Cold sweat (10009866)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hyperhidrosis (10020642)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Rash (10037844)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	3	0.3	0.1	0.9	3	1.0	0.2	2.9
	Skin ulcer (10040943)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Urticaria (10046735)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Surgical and medical procedures (10042613)	Sinus operation (10062245)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
At least one symptom = at least one symptom reported (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose

n/% = number/percentage of subjects reporting the symptom at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Supplement 69 Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		7	0.8	0.3	1.5	5	0.5	0.2	1.3	3	0.3	0.1	0.9	4	1.3	0.4	3.4
Ear and labyrinth disorders (10013993)	Middle ear effusion (10062545)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Gastritis (10017853)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Vomiting (10047700)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
General disorders and administration site conditions (10018065)	Fatigue (10016256)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Influenza like illness (10022004)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site warmth (10022112)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pyrexia (10037660)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Infections and infestations (10021881)	Lower respiratory tract infection (10024968)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pneumonia (10035664)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Viral infection (10047461)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Joint range of motion decreased (10048706)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Grand mal convulsion (10018659)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Psychomotor hyperactivity (10037211)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
At least one symptom = at least one symptom reported (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Supplement 70 **Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the entire study period (TVC)**

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		346	37.1	34.0	40.3	335	36.1	33.0	39.2	350	37.6	34.4	40.8	147	48.8	43.1	54.6
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	4	1.3	0.4	3.4
	Iron deficiency anaemia (10022972)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Lymphadenitis (10025188)	3	0.3	0.1	0.9	2	0.2	0.0	0.8	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Lymphadenopathy (10025197)	2	0.2	0.0	0.8	5	0.5	0.2	1.3	4	0.4	0.1	1.1	1	0.3	0.0	1.8
	Neutropenia (10029354)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Cardiac disorders (10007541)	Bradycardia (10006093)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tachycardia (10043071)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Congenital, familial and genetic disorders (10010331)	Dacryostenosis congenital (10011850)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Keratosis follicular (10023369)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Stickler's syndrome (10063402)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Vitello-intestinal duct remnant (10066969)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Von willebrand's disease (10047715)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Ear and labyrinth disorders (10013993)	Allergic otitis media (10061557)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Auricular swelling (10003800)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Cerumen impaction (10050337)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	1	0.1	0.0	0.6	4	1.3	0.4	3.4
	Ear discomfort (10052137)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Ear pain (10014020)	3	0.3	0.1	0.9	5	0.5	0.2	1.3	6	0.6	0.2	1.4	1	0.3	0.0	1.8
	Middle ear effusion (10062545)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Otorrhoea (10033101)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tinnitus (10043882)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tympanic membrane hyperaemia (10052154)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Vertigo (10047340)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Endocrine disorders (10014698)	Precocious puberty (10058084)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Eye disorders (10015919)	Chalazion (10008388)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Conjunctivitis (10010741)	15	1.6	0.9	2.6	14	1.5	0.8	2.5	10	1.1	0.5	2.0	7	2.3	0.9	4.7
	Conjunctivitis allergic (10010744)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eye discharge (10015915)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Eye movement disorder (10061129)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eye pruritus (10052140)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Myopia (10028651)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Refraction disorder (10038264)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Retinal degeneration (10038845)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Scleral degeneration (10061509)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Visual impairment (10047571)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Gastrointestinal disorders (10017947)	Abdominal distension (10000060)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Abdominal pain (10000081)	6	0.6	0.2	1.4	8	0.9	0.4	1.7	9	1.0	0.4	1.8	0	0.0	0.0	1.2
	Abdominal pain lower (10000084)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Abdominal pain upper (10000087)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Anal fissure (10002153)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Aphthous stomatitis (10002958)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Colitis (10009887)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Constipation (10010774)	5	0.5	0.2	1.2	5	0.5	0.2	1.3	7	0.8	0.3	1.5	1	0.3	0.0	1.8
	Dental caries (10012318)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Diarrhoea (10012735)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	3	0.3	0.1	0.9	6	2.0	0.7	4.3
	Dyspepsia (10013946)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Enteritis (10014866)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	1	0.1	0.0	0.6	2	0.7	0.1	2.4
	Faecal incontinence (10016092)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Food poisoning (10016952)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gastritis (10017853)	3	0.3	0.1	0.9	3	0.3	0.1	0.9	5	0.5	0.2	1.2	2	0.7	0.1	2.4
	Gastrointestinal disorder (10017944)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Gastrointestinal inflammation (10064147)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gastrooesophageal reflux disease (10017885)	3	0.3	0.1	0.9	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Gingivitis (10018292)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Lip pain (10024561)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Mouth ulceration (10028034)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nausea (10028813)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Proctalgia (10036772)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Toothache (10044055)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Vomiting (10047700)	8	0.9	0.4	1.7	7	0.8	0.3	1.5	6	0.6	0.2	1.4	6	2.0	0.7	4.3
General disorders and administration site conditions (10018065)	Chest pain (10008479)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Chronic fatigue syndrome (10008874)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Cyst (10011732)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Device leakage (10012587)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Fatigue (10016256)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Influenza like illness (10022004)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Injection site pruritus (10022093)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site reaction (10022095)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Injection site vesicles (10022111)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injection site warmth (10022112)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Malaise (10025482)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Mass (10026865)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Oedema peripheral (10030124)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Pain (10033371)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Pyrexia (10037660)	10	1.1	0.5	2.0	18	1.9	1.2	3.0	13	1.4	0.7	2.4	16	5.3	3.1	8.5
Hepatobiliary disorders (10019805)	Biliary dyskinesia (10056529)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Immune system disorders (10021428)	Allergy to animal (10001742)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Anaphylactic reaction (10002198)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Drug hypersensitivity (10013700)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Food allergy (10016946)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	House dust allergy (10057631)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hypersensitivity (10020751)	3	0.3	0.1	0.9	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Seasonal allergy (10048908)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Selective iga immunodeficiency (10039915)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Infections and infestations (10021881)	Abscess (10000269)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Abscess limb (10050473)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Abscess neck (10053576)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Acarodermatitis (10063409)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Acute sinusitis (10001076)	5	0.5	0.2	1.2	5	0.5	0.2	1.3	4	0.4	0.1	1.1	1	0.3	0.0	1.8
	Acute tonsillitis (10001093)	3	0.3	0.1	0.9	3	0.3	0.1	0.9	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Bacterial infection (10060945)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Beta haemolytic streptococcal infection (10052100)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Body tinea (10005913)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Bronchiolitis (10006448)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	4	1.3	0.4	3.4
	Bronchitis (10006451)	23	2.5	1.6	3.7	21	2.3	1.4	3.4	19	2.0	1.2	3.2	5	1.7	0.5	3.8
	Bronchopneumonia (10006469)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Candidiasis (10007152)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Carbuncle (10007247)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Cellulitis (10007882)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Chronic sinusitis (10009137)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Conjunctivitis infective (10010742)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Conjunctivitis viral (10010755)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Croup infectious (10011416)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	3	0.3	0.1	0.9	9	3.0	1.4	5.6
	Cystitis (10011781)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	3	0.3	0.1	0.9	1	0.3	0.0	1.8
	Ear infection (10014011)	5	0.5	0.2	1.2	4	0.4	0.1	1.1	6	0.6	0.2	1.4	9	3.0	1.4	5.6
	Enteritis infectious (10058839)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Enterobiasis (10014881)	3	0.3	0.1	0.9	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Enterovirus infection (10014909)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Epstein-barr virus infection (10015108)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Erythema infectiosum (10015214)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Eye infection (10015929)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Eyelid infection (10015988)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Folliculitis (10016936)	4	0.4	0.1	1.1	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Fungal infection (10017533)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Fungal skin infection (10017543)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Furuncle (10017553)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Gastroenteritis (10017888)	22	2.4	1.5	3.6	16	1.7	1.0	2.8	19	2.0	1.2	3.2	6	2.0	0.7	4.3
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gastroenteritis viral (10017918)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	4	1.3	0.4	3.4
	Hand-foot-and-mouth disease (10019113)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Herpangina (10019936)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Herpes zoster (10019974)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Impetigo (10021531)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Infectious mononucleosis (10021914)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Influenza (10022000)	8	0.9	0.4	1.7	7	0.8	0.3	1.5	12	1.3	0.7	2.2	0	0.0	0.0	1.2
	Laryngitis (10023874)	9	1.0	0.4	1.8	10	1.1	0.5	2.0	7	0.8	0.3	1.5	0	0.0	0.0	1.2
	Lice infestation (10024424)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Lobar pneumonia (10024738)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Localised infection (10024774)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Lower respiratory tract infection (10024968)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Mastitis (10026883)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Molluscum contagiosum (10027807)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Mycoplasma infection (10061300)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nasopharyngitis (10028810)	54	5.8	4.4	7.5	50	5.4	4.0	7.0	44	4.7	3.5	6.3	4	1.3	0.4	3.4
	Onychomycosis (10030338)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Oral candidiasis (10030963)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Oral herpes (10067152)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Otitis externa (10033072)	3	0.3	0.1	0.9	3	0.3	0.1	0.9	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Otitis media (10033078)	27	2.9	1.9	4.2	21	2.3	1.4	3.4	31	3.3	2.3	4.7	37	12.3	8.8	16.5
	Otitis media acute (10033079)	9	1.0	0.4	1.8	8	0.9	0.4	1.7	11	1.2	0.6	2.1	5	1.7	0.5	3.8
	Otitis media chronic (10033081)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Parasitic gastroenteritis (10067720)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Paronychia (10034016)	1	0.1	0.0	0.6	3	0.3	0.1	0.9	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Pertussis (10034738)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pharyngitis (10034835)	39	4.2	3.0	5.7	34	3.7	2.5	5.1	35	3.8	2.6	5.2	4	1.3	0.4	3.4
	Pharyngitis bacterial (10057869)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pharyngitis streptococcal (10034839)	28	3.0	2.0	4.3	15	1.6	0.9	2.6	25	2.7	1.7	3.9	5	1.7	0.5	3.8
	Pharyngotonsillitis (10049140)	10	1.1	0.5	2.0	9	1.0	0.4	1.8	12	1.3	0.7	2.2	0	0.0	0.0	1.2
	Pneumonia (10035664)	7	0.8	0.3	1.5	6	0.6	0.2	1.4	6	0.6	0.2	1.4	7	2.3	0.9	4.7
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pneumonia primary atypical (10035730)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Pneumonia viral (10035737)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Pyelonephritis (10037596)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Respiratory syncytial virus infection (10061603)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Respiratory tract infection (10062352)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	8	0.9	0.4	1.7	1	0.3	0.0	1.8
	Rhinitis (10039083)	4	0.4	0.1	1.1	3	0.3	0.1	0.9	3	0.3	0.1	0.9	3	1.0	0.2	2.9
	Roseola (10039222)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Scarlet fever (10039587)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Sepsis (10040047)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Sinusitis (10040753)	20	2.1	1.3	3.3	19	2.0	1.2	3.2	16	1.7	1.0	2.8	7	2.3	0.9	4.7
	Skin bacterial infection (10052891)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Streptococcal infection (10061372)	4	0.4	0.1	1.1	5	0.5	0.2	1.3	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Subcutaneous abscess (10042343)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Tinea capitis (10043866)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tinea infection (10060889)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tinea pedis (10043873)	0	0.0	0.0	0.4	3	0.3	0.1	0.9	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tonsillitis (10044008)	12	1.3	0.7	2.2	16	1.7	1.0	2.8	18	1.9	1.1	3.0	1	0.3	0.0	1.8
	Tooth abscess (10044016)	0	0.0	0.0	0.4	3	0.3	0.1	0.9	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tooth infection (10048762)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tracheitis (10044302)	2	0.2	0.0	0.8	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tracheobronchitis (10044314)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Upper respiratory tract infection (10046306)	64	6.9	5.3	8.7	64	6.9	5.3	8.7	75	8.0	6.4	10.0	40	13.3	9.7	17.7
	Urinary tract infection (10046571)	9	1.0	0.4	1.8	3	0.3	0.1	0.9	9	1.0	0.4	1.8	1	0.3	0.0	1.8
	Urinary tract infection bacterial (10054088)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Vaginal infection (10046914)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Varicella (10046980)	2	0.2	0.0	0.8	5	0.5	0.2	1.3	4	0.4	0.1	1.1	0	0.0	0.0	1.2
	Viral infection (10047461)	16	1.7	1.0	2.8	14	1.5	0.8	2.5	8	0.9	0.4	1.7	16	5.3	3.1	8.5
	Viral pharyngitis (10047473)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Viral rash (10047476)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Viral rhinitis (10064948)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Viral upper respiratory tract infection (10047482)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	0.4	5	1.7	0.5	3.8
	Vulvovaginitis (10047794)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Wound infection staphylococcal (10059442)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Injury, poisoning and procedural complications (10022117)	Accidental overdose (10000381)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Animal bite (10002515)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Ankle fracture (10002544)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Arthropod bite (10003399)	3	0.3	0.1	0.9	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Back injury (10003986)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Bite (10004966)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Burns second degree (10006802)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Concussion (10010254)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Contusion (10050584)	5	0.5	0.2	1.2	2	0.2	0.0	0.8	6	0.6	0.2	1.4	2	0.7	0.1	2.4
	Documented hypersensitivity to administered drug (10064372)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Excoriation (10049796)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Eye penetration (10015960)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Face injury (10050392)	0	0.0	0.0	0.4	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Facial bones fracture (10016042)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Femur fracture (10016454)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Foot fracture (10016970)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Forearm fracture (10016997)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Foreign body (10070245)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Hand fracture (10019114)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Head injury (10019196)	5	0.5	0.2	1.2	0	0.0	0.0	0.4	2	0.2	0.0	0.8	2	0.7	0.1	2.4
	Humerus fracture (10020462)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Injury (10022116)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint dislocation (10023204)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Joint injury (10060820)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint sprain (10023229)	7	0.8	0.3	1.5	3	0.3	0.1	0.9	5	0.5	0.2	1.2	0	0.0	0.0	1.2
	Laceration (10023572)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	4	0.4	0.1	1.1	2	0.7	0.1	2.4
	Limb injury (10061225)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Lip injury (10055082)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Mouth injury (10049294)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Muscle injury (10028314)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Muscle strain (10050031)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Radius fracture (10037802)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Reaction to previous exposure to any vaccine (10066904)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Splinter (10041662)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Stress fracture (10042212)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Superficial injury of eye (10042530)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Thermal burn (10053615)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tibia fracture (10043827)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Tooth injury (10044043)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Traumatic brain injury (10060690)	0	0.0	0.0	0.4	4	0.4	0.1	1.1	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Upper limb fracture (10061394)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Wound (10052428)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Wrist fracture (10048049)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Investigations (10022891)	Cardiac murmur (10007586)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Electrocardiogram qt prolonged (10014387)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Intraocular pressure increased (10022806)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Parasite stool test negative (10033904)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Weight increased (10047899)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hypovolaemia (10021137)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Obesity (10029883)	2	0.2	0.0	0.8	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	3	0.3	0.1	0.9	3	0.3	0.1	0.9	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Back pain (10003988)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Chondropathy (10061762)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Connective tissue disorder (10061087)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Costochondritis (10011219)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Hip deformity (10061209)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Intervertebral disc protrusion (10050296)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint effusion (10023215)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Joint swelling (10023232)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Muscle contracture (10062575)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Muscle rigidity (10028330)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Muscle spasms (10028334)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Musculoskeletal disorder (10048592)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Myalgia (10028411)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Neck pain (10028836)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Osteochondrosis (10031233)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Pain in extremity (10033425)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	4	0.4	0.1	1.1	1	0.3	0.0	1.8
	Sever's disease (10050089)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Synovitis (10042868)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tendonitis (10043255)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Torticollis (10044074)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Eyelid tumour (10050497)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Melanocytic naevus (10027145)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Neoplasm (10028980)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Skin papilloma (10040907)	2	0.2	0.0	0.8	5	0.5	0.2	1.3	3	0.3	0.1	0.9	0	0.0	0.0	1.2
Nervous system disorders (10029205)	Altered state of consciousness (10001854)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Cerebrovascular accident (10008190)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Convulsion (10010904)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Dizziness (10013573)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Febrile convulsion (10016284)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Grand mal convulsion (10018659)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Headache (10019211)	5	0.5	0.2	1.2	5	0.5	0.2	1.3	5	0.5	0.2	1.2	0	0.0	0.0	1.2
	Lethargy (10024264)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Migraine (10027599)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Migraine without aura (10052787)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Simple partial seizures (10040703)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Speech disorder (10041466)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Syncope (10042772)	2	0.2	0.0	0.8	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tension headache (10043269)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
Psychiatric disorders (10037175)	Abnormal behaviour (10061422)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Adjustment disorder (10061621)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Affective disorder (10001443)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Anxiety (10002855)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Asperger's disorder (10003484)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Attention deficit/hyperactivity disorder (10003736)	6	0.6	0.2	1.4	4	0.4	0.1	1.1	7	0.8	0.3	1.5	0	0.0	0.0	1.2
	Depression (10012378)	3	0.3	0.1	0.9	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Dysphemia (10054964)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Eating disorder (10014062)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Emotional disorder (10014551)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Insomnia (10022437)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Learning disorder (10061265)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Sleep terror (10041010)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Suicidal ideation (10042458)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Tic (10043833)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Trichotillomania (10044629)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Renal and urinary disorders (10038359)	Dysuria (10013990)	2	0.2	0.0	0.8	2	0.2	0.0	0.8	3	0.3	0.1	0.9	0	0.0	0.0	1.2
	Enuresis (10014928)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Haematuria (10018867)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Hydronephrosis (10020524)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Reproductive system and breast disorders (10038604)	Amenorrhoea (10001928)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Balanitis (10004073)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Breast mass (10006272)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Breast pain (10006298)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Gynaecomastia (10018800)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Menstruation irregular (10027339)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Ovarian cyst (10033132)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Posthitis (10036379)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Prepuce redundant (10036624)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Vaginal discharge (10046901)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Asthma (10003553)	9	1.0	0.4	1.8	11	1.2	0.6	2.1	11	1.2	0.6	2.1	11	3.7	1.8	6.4
	Asthma exercise induced (10003557)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Asthmatic crisis (10064823)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Bronchial hyperreactivity (10066091)	9	1.0	0.4	1.8	9	1.0	0.4	1.8	4	0.4	0.1	1.1	5	1.7	0.5	3.8
	Bronchitis chronic (10006458)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Bronchospasm (10006482)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Cough (10011224)	31	3.3	2.3	4.7	29	3.1	2.1	4.5	27	2.9	1.9	4.2	21	7.0	4.4	10.5
	Epistaxis (10015090)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Nasal congestion (10028735)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Nasal disorder (10062209)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Nasal turbinate abnormality (10052354)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Oropharyngeal pain (10068319)	7	0.8	0.3	1.5	3	0.3	0.1	0.9	5	0.5	0.2	1.2	1	0.3	0.0	1.8
	Pneumonitis (10035742)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Productive cough (10036790)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Respiratory distress (10038687)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Rhinitis allergic (10039085)	8	0.9	0.4	1.7	16	1.7	1.0	2.8	9	1.0	0.4	1.8	3	1.0	0.2	2.9
	Rhinorrhoea (10039101)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	7	2.3	0.9	4.7
	Rhonchi (10039109)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Sinus congestion (10040742)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Sleep apnoea syndrome (10040979)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Snoring (10041235)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Tonsillar hypertrophy (10044003)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Wheezing (10047924)	2	0.2	0.0	0.8	3	0.3	0.1	0.9	2	0.2	0.0	0.8	2	0.7	0.1	2.4
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	0	0.0	0.0	0.4	3	0.3	0.1	0.9	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Alopecia (10001760)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Angioedema (10002424)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Blister (10005191)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Dandruff (10011859)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Dermal cyst (10012426)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Dermatitis (10012431)	3	0.3	0.1	0.9	5	0.5	0.2	1.3	2	0.2	0.0	0.8	1	0.3	0.0	1.8
	Dermatitis atopic (10012438)	1	0.1	0.0	0.6	4	0.4	0.1	1.1	6	0.6	0.2	1.4	4	1.3	0.4	3.4
	Dermatitis contact (10012442)	1	0.1	0.0	0.6	2	0.2	0.0	0.8	5	0.5	0.2	1.2	0	0.0	0.0	1.2
	Dermatitis diaper (10012444)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Eczema (10014184)	2	0.2	0.0	0.8	4	0.4	0.1	1.1	1	0.1	0.0	0.6	2	0.7	0.1	2.4
	Erythema (10015150)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hyperhidrosis (10020642)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Ingrowing nail (10022013)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Keratosis pilaris (10066295)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Lichen nitidus (10024428)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Nail disorder (10028694)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Petechiae (10034754)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Pityriasis (10035110)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Prurigo (10037083)	0	0.0	0.0	0.4	2	0.2	0.0	0.8	2	0.2	0.0	0.8	0	0.0	0.0	1.2
	Pruritus (10037087)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Psoriasis (10037153)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Rash (10037844)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	6	0.6	0.2	1.4	9	3.0	1.4	5.6
	Seborrhoeic dermatitis (10039793)	1	0.1	0.0	0.6	1	0.1	0.0	0.6	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Skin maceration (10048625)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Skin ulcer (10040943)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	1.2
	Urticaria (10046735)	8	0.9	0.4	1.7	5	0.5	0.2	1.3	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Vitiligo (10047642)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Social circumstances (10041244)	Exposure to communicable disease (10049711)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2
Surgical and medical procedures (10042613)	Abscess drainage (10000279)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8

		QIV1 N = 932				TIV-VB N = 929				TIV-YB N = 932				QIV2 N = 301			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Adenotonsillectomy (10001256)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.3	0.0	1.8
	Ear tube insertion (10057900)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.7	0.1	2.4
	Joint fluid drainage (10066994)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.3	0.0	1.8
	Tooth extraction (10062132)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Wisdom teeth removal (10047991)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	1.2
Vascular disorders (10047065)	Haematoma (10018852)	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	1.2
	Hypertension (10020772)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	1.2

QIV1 = Flu Q-QIV (3 - 17 years)
TIV-VB = Fluarix TIV Victoria B strain (3 - 17 years)
TIV-YB = Fluarix TIV Yamagata B strain (3 - 17 years)
QIV2 = Flu Q-QIV (6 - 35 months)
At least one symptom = at least one symptom reported (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting at least once the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

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12. STUDY REPORT AUTHORS /CONTRIBUTING AUTHORS

Scientific Writer: (b) (6)

Project Statistician: (b) (6)

Global Study Manager: (b) (6)

Central Safety Contact: (b) (6)

Clinical Development Manager: (b) (6)

Regulatory Affairs representative: (b) (6)

N + 1 of CDM: (b) (6)

13. SERIOUS ADVERSE EVENTS

13.1. SAE Summary Table

Table 51 Listing of SAEs reported during the entire study period (All enrolled subjects)

Group	Sub. No.	Case Id	Age at onset (Year)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
QIV1	(b) (6)		9	M	Hypertension	Hypertension	Vascular disorders	HO	1	154	6	3	N	Recovered/resolved with sequelae
			9		Mesenteric adenitis	Lymphadenitis	Blood and lymphatic system disorders	HO	1	156	4	3	N	Recovered/resolved
	(b) (6)		13	F	Worsening depression	Depression	Psychiatric disorders	HO	1	5	6	3	N	Recovered/resolved
	(b) (6)		5	F	Intake of antihistamines	Accidental overdose	Injury, poisoning and procedural complications	HO	2	64	2	1	N	Recovered/resolved
TIV-VB	(b) (6)		4	M	Anaphylactic reaction due to unspecified food	Anaphylactic reaction	Immune system disorders	ER	2	103	1	2	N	Recovered/resolved
			4		Allergic reaction	Hypersensitivity	Immune system disorders	ER	2	125	6	2	N	Recovered/resolved
			4		Urticaria	Urticaria	Skin and subcutaneous tissue disorders	ER	2	103	6	2	N	Recovered/resolved
			4		Urticaria	Urticaria	Skin and subcutaneous tissue disorders	ER	2	125	6	2	N	Recovered/resolved
	(b) (6)		17	F	Biliary dyskinesia	Biliary dyskinesia	Hepatobiliary disorders	HO	1	1	145	3	N	Recovered/resolved
			17		Meckel diverticulum	Vitello-intestinal duct remnant	Congenital, familial and genetic disorders	HO	1	1	145	3	N	Recovered/resolved
	(b) (6)		15	M	Anxiety reaction	Anxiety	Psychiatric disorders	ER	1	104	1	2	N	Recovered/resolved
			15		Depression-exacerbation	Depression	Psychiatric disorders	ER	1	104	.	2	N	Not recovered/not resolved

Group	Sub. No.	Case Id	Age at onset (Year)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
			15		Suicidal ideation	Suicidal ideation	Psychiatric disorders	ER	1	104	1	2	N	Recovered/resolved
		(b) (6)	17	F	Pneumonia	Pneumonia	Infections and infestations	HO	1	116	7	1	N	Recovered/resolved
			4	F	Acute gastroenteritis	Gastroenteritis	Infections and infestations	HO	2	54	9	2	N	Recovered/resolved
			3	M	Craneoencephalic trauma	Traumatic brain injury	Injury, poisoning and procedural complications	HO	1	7	2	3	N	Recovered/resolved
TIV-YB			11	M	Face fracture	Facial bones fracture	Injury, poisoning and procedural complications	HO	1	8	7	3	N	Recovered/resolved
			11		Head injury	Head injury	Injury, poisoning and procedural complications	HO	1	8	7	3	N	Recovered/resolved
			4	M	Rotovirus	Gastroenteritis rotavirus	Infections and infestations	HO	2	125	4	3	N	Recovered/resolved
			16	M	Dislocated glenohumeral joint right side	Joint dislocation	Injury, poisoning and procedural complications	ER	1	158	20	3	N	Recovered/resolved
			12	M	Angioedema	Angioedema	Skin and subcutaneous tissue disorders	MD	1	0	7	2	Y	Recovered/resolved
			12		Acute conjunctivitis	Conjunctivitis	Eye disorders	MD	1	0	7	1	Y	Recovered/resolved
			3	M	Bronchopneumonia	Bronchopneumonia	Infections and infestations	HO	1	88	26	1	N	Recovered/resolved
			3		Volume depletion	Hypovolaemia	Metabolism and nutrition disorders	HO	1	88	8	1	N	Recovered/resolved
			3		Influenza	Influenza	Infections and infestations	HO	1	81	15	1	N	Recovered/resolved

Group	Sub. No.	Case Id	Age at onset (Year)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
QIV2	(b) (6)		1	F	Grand mal seizure	Grand mal convulsion	Nervous system disorders	ER	1	0	1	3	Y	Recovered/resolved
			2	M	Asthma	Asthma	Respiratory, thoracic and mediastinal disorders	HO	2	45	5	3	N	Recovered/resolved
			3	F	asthma exacerbation	Asthma	Respiratory, thoracic and mediastinal disorders	HO	1	19	3	3	N	Recovered/resolved
			3		Right lower lobe pneumonia	Lobar pneumonia	Infections and infestations	HO	1	19	3	1	N	Recovered/resolved
			2	M	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	18	1	3	Y	Recovered/resolved
			0	F	Respiratory syncytial virus	Respiratory syncytial virus infection	Infections and infestations	ER	2	6	10	3	N	Recovered/resolved
			1	F	Gastroenteritis	Gastroenteritis	Infections and infestations	HO	2	121	8	3	N	Recovered/resolved
			3	F	Foreign body in esophagus	Foreign body	Injury, poisoning and procedural complications	ER	2	43	2	2	N	Recovered/resolved
			3	M	Asthma	Asthma	Respiratory, thoracic and mediastinal disorders	HO	2	138	23	3	N	Recovered/resolved
			3		Viral pneumonia	Pneumonia viral	Infections and infestations	HO	2	136	25	3	N	Recovered/resolved

13.2. CIOMS reports

13.2.1. Serious Adverse Events CIOMS

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		F	16Oct2010

7. & 13. DESCRIBE EVENT(S)

Grand mal convulsion

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

On (b) (6), four hours after the 1st dose of Flu Quadrivalent split without adjuvant Quebec, this 21-month-old subject experienced grand mal seizure. The event was clinically significant (or requiring intervention). The subject was treated with diphenhydramine hydrochloride. The event resolved on (b) (6). The investigator considered that there was a reasonable possibility that the grand mal seizure may have been caused by Flu Quadrivalent split without adjuvant Quebec.

Investigator Comments : Child received study vaccine at 12:00. At 1600, child was playing in the front yard at her home when she fell

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION	17. NDICATION(S) FOR USE	18. THERAPY DATES (From / To)	19. THERAPY DURATION
Unknown	Intramuscular	PROPHYLAXIS	(b) (6)	1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION	17. NDICATION(S) FOR USE	18. THERAPY DATES (From / To)	19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0013888A

24c. DATE RECEIVED: 17NOV2010

DATE OF REPORT: 22NOV2010

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☒ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

to the ground, shaking, eyes fixed and deviated to the left and stopped breathing. She also had a rash on her hands and inner thighs. Mom called the paramedics and was taken to the ER. The ER doctor evaluated her and gave her Benadryl, which resoved the rash within hours. She was sent home from the ER. ER doctor accessed subject's causality. PI and Sub-I were not available during event, but have been notified as of 10/18/2010. PI will look at and review SAE screens. No history of seizures or febrile seizures. No family history. The subject takes no medications. The subject had no fever and no pain, swelling, redness at injection site. Child previously healthy and no neuro testing done. Grand mal seizure lasted 2-3 minutes.Temp 97.9F, BP 119/78, pulse 165bpm, respiratory rate 33. Physical exam was normal in the ER. Serious adverse event was discussed with Dr. Chatterjee who assessed causality as related on 18Oct2010 before event was recorded as an SAE.
Update 17NOV2010- Per parent, subject fall was beginning of convulsion-was not a fall that would have resulted in a head injury. Per Dr.Chatterjee, the rash described was not a rash that would be associated with anaphylaxis. She does not feel there is a reasonable possibility of this being an anaphylactic reaction. There were no other signs or symptoms, no fever and no additional patient history.

Lab tests dated (b) (6) :
RDW SD : 35.2 FL
RD CV : 12.8%
NRBC : 0 WBC (normal range 0-100)
Imm. Gran : 0.2%
Imm. Gran :0.02 thous
Diff. type : automated

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Alanine aminotransferase	(b) (6)	17U/L	5	35
Albumin		4.4g/dL	3.8	5.4
Alkaline phosphatase		200U/L	50	350
Aspartate aminotransferase		33U/L	10	40
BUN		15mg/dL	6	22
Basophils		0.4%	0.0	1.0
Basophils		0.05Thous		
Bilirubin unconjugated		0.1mg/dL	0.0	1.1
Blood chromium		0.0mg/dL	0.0	0.3
Calcium		9.6mg/dL	8.8	10.5
Carbon dioxide		22mmol/L	17	25
Chloride		104mmol/L	98	108
Creatinine		0.29mg/dL	0.20	0.62
Eosinophils		1.9%	0.0	3.0
Eosinophils		0.24Thous		
Glucose		101mg/dL	70	110
Hematocrit		32.6%	31.2	37.2
Hemoglobin		11.5g/dL	10.4	12.4
Lymphocytes		5.32Thous	1.2	7.0
Lymphocytes		41.5%	20.0	63.0
MCH		27.0pg	23.5	27.6
MCHC		35.3g/dL	31.8	34.8
Mean corpuscular volume		76.5fl	71.5	81.8
Mean platelet volume		8.6fL		
Monocytes		7.9%	4.0	11.0
Monocytes		1.01Thous		
Neutrophils		6.19Thous	1.8	9.1
Neutrophils		48.1%	22.0	67.0
Platelet count		348Thous	229	465
Potassium		4.3mmol/L	3.5	5.5
Protein		7.2g/dL	6.2	8.7
Red blood cell count		4.26Million	4.10	4.90
Sodium		138mmol/L	135	148
White blood cell count		12.83Thous	6.40	15.00

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Depression

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

Medical conditions at the time of the event included bulimia and depression. Concomitant medications included Zoloft.

On (b) (6), five days after the 1st dose of flu quadrivalent split quebec, this 13-year-old subject developed worsened depression. The subject was hospitalised. The event resolved on 12 October 2010. The investigator considered that there was no reasonable possibility that the worsened depression may have been caused by Flu Quadrivalent split without adjuvant Quebec and that the event was possibly due to the subject's medical condition.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Sertraline hydrochloride 2010 - Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0014136A

24c. DATE RECEIVED: 02MAR2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Investigator Comments : The subject was at an outpatient therapy session and she would not agree that she would keep herself safe. The therapist sent her to the Emergency department for evaluation. She was admitted for worsening depression. The subject is having difficulty in school and is restricting her food. She has a history from Oct 2009 of attempting to over dose on various pills. The pills were ingested then she vomited.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
BULIMIA	2008	Unknown	Yes
DEPRESSION	2008	Unknown	Yes

INTERNATIONAL EVENT REPORT

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Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Asthma, Lobar pneumonia

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

Medical conditions at the time of the event included asthma. Concomitant medications included Flovent and Albuterol.

On (b) (6), 19 days after the 1st dose of flu quadrivalent split quebec, this three-year-old subject developed lower lobe pneumonia and exacerbation of asthma. The subject was hospitalised. The subject was treated with prednisolone, levosalbutamol, salbutamol sulphate, ipratropium bromide and azithromycin. The events resolved on 25 October 2010. The investigator considered that there was no reasonable possibility that the exacerbation of asthma and lower lobe pneumonia may have been caused by Flu

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Salbutamol sulphate
Fluticasone propionate

(b) (6) - Unknown
- Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0014262A

24c. DATE RECEIVED: 16JUN2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0014262A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Quadrivalent split without adjuvant Quebec and that the events were possibly due to the subject’s medical condition.

Investigator Comments : Subject started sounding congested (nasal, chest) on early am 23OCT10. Subject received updrafts of albuterol X3 but symptoms persisted and she proceeded to the ER at Children’s. Upon ER presentation, her pulse ox was 90% with labored and retracted breathing. She received albuterol updraft Q 20 mins X4 then a dose of oral steroids. Her breathing improved but her pulse ox remained low. A chest X-ray was done and she was admitted for observation. She continues receiving updrafts Q2hrs and oral steroid daily. By Sunday evening her condition had improved and updrafts were stopped. She was discharged the next evening. Subject recovered.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
ASTHMA	May2009	Unknown	Yes

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Taiwan, ROC	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Angioedema, Conjunctivitis

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-YB (Lot DFLUA039A).

On (b) (6), same day after the 1st dose of Blinded vaccine, this 12-year-old subject developed angioedema and acute conjunctivitis. The events were clinically significant (or requiring intervention). The subject was treated with ambroxol, buclizine, levocetirizine hydrochloride and fluorometholone. The events resolved on 12 November 2010. The investigator considered that there was a reasonable possibility that the angioedema and

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix YB Injection DFLUA039A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0014352A

24c. DATE RECEIVED	DATE OF REPORT
16SEP2011	22SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☒ FOLLOW-UP

R0014352A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

acute conjunctivitis may have been caused by investigational product and that the events were possibly due to allergic reaction.

Investigator Comments : The subject received study vaccine on (b) (6) . Chest tightness developed at night thereafter. On the next day, bilateral puffy eyelids were noted. He denied fever, short of breath or skin rash in these two days. At outpatient department on (b) (6) , Angioedema and acute conjunctivitis were impressed. Symptomatic medication was given. Discomfort symptoms resolved on 12Nov2010.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: 03006 Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Febrile convulsion

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

On (b) (6) 0, 18 days after the 1st dose of flu quadrivalent split quebec, this 30-month-old subject developed febrile seizure. The event was clinically significant (or requiring intervention). The subject was treated with ibuprofen. The event resolved on 03 November 2010. The investigator considered that there was a reasonable possibility that the febrile seizure may have been caused by Flu Quadrivalent split without adjuvant Quebec.

Investigator Comments : this child developed fever on the morning of (b) (6) and had a generalized seizure and collapsed while holding on to the mother's leg. According to the mother the child

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☒ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To): (b) (6) 0

19. THERAPY DURATION: 1 Days

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)

19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0014422A

24c. DATE RECEIVED: 15DEC2010

DATE OF REPORT: 20DEC2010

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☒ FOLLOW-UP

R0014422A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

fell down, his eyes were rolled back and was shaking all four limbs. It was not possible to communicate with the child. The seizure lasted for about 15 minutes but the child could not be aroused. The ambulance was called and the child was taken to the emergency room. The temperature recorded in the ambulance was 39.2 C. There was no incontinence. The child did not have any signs of infection prior to the onset of febrile seizure. There is no prior history of seizure and there is no family history of seizure or febrile seizure. The child was given Advil for fever and the child was afebrile before he was sent home from the emergency room. An EEG is being arranged.
The investigator considers this febrile seizure an important medical event that did not result in hospitalization. The subject will continue in the study for safety follow-up.
EEG conducted (b) (6) normal.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Urinalysis	(b) (6)	NEG		
Urine culture		NEG		

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Head injury, Facial bones fracture

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-YB (Lot DFLUA039A).

On (b) (6), eight days after the 1st dose of Blinded vaccine, this 11-year-old subject experienced head injury and facial fracture. The subject was hospitalised. The events resolved on 29 October 2010. The investigator considered that there was no reasonable possibility that the head injury and facial fracture may have been caused by investigational product and that the events were possibly due to trauma.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix YB Injection DFLUA039A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)

19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0014566A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0014566A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Investigator Comments : Head trauma secondary to a bicycle accident. Resulted in facial fractures. CT scans completed and subject was observed for 23 hours. CT results = nondisplaced hairline fractures through the left cribriform plate, left frontal sinus and left lamina papyracea. Preseptal emphysema and edema surrounding left orbit with postseptal extraconal air tracking along the left orbital roof. Punctate foci of intracranial air along left inferior frontal convexity.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Spain	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Traumatic brain injury

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

On (b) (6), seven days after the 1st dose of Blinded vaccine, this three-year-old subject experienced cranioencephalic trauma. The subject was hospitalised. The event resolved on 04 December 2010. The investigator considered that there was no reasonable possibility that the cranioencephalic trauma may have been caused by investigational product and that the event was

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0014951A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0014951A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

possibly due to trauma.

Investigator Comments : The subject come to the hospital due to a craneoencephalic trauma due to a fall. He is hospitalized for observation, no bleeding, no vomiting, no loss of consciousness. Good evolution.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Respiratory syncytial virus infection

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

Medical conditions at the time of the event included gastroesophageal reflux and weight decrease.

On (b) (6), six days after the 2nd dose of flu quadrivalent split quebec, this 10-month-old subject developed respiratory syncytial virus. The event was clinically significant (or requiring intervention). The subject was treated with paracetamol, ibuprofen, nebulizer, salbutamol sulphate and fluticasone propionate. The event resolved on 05 January 2011. The investigator considered that there was no reasonable possibility that the respiratory syncytial

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0015580A

24c. DATE RECEIVED: 23JUN2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0015580A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

virus may have been caused by Flu Quadrivalent split without adjuvant Quebec and that the event was possibly due to viral infection and to the subject's medical conditions.

Investigator Comments : (b) (6), subject had nasal discharge, cough, sneezing and uncontrolled fever. (b) (6), parents took subject into emergency for uncontrolled fever and dyspnea. In emergency subject had chest x-ray done, nasal swab for RSV (Respiratory Syncytial Virus) and nebulizer once for dyspnea. Medications given for uncontrolled fever. Subject discharged home from emergency same day. On (b) (6) subject was back in emergency with fever and dyspnea. Nasal swab results from previous emergency visit came back positive for Respiratory Syncytial Virus. Subject had one treatment with nebulizer for dyspnea and then was discharged from emergency with two inhalers to be used till the 05 Jan. 2011. By 05 Jan. 2011, parent stated that Respiratory Syncytial Virus symptoms were resolved. No results from chest x-ray.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
NASAL SWAB Respiratory Syncytial Virus	(b) (6)	POSITIVEUNK	UNK	UNK

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
WEIGHT DECREASE	07Feb2010	Unknown	Yes
GASTROESOPHAGEAL REFLUX	07Feb2010	Unknown	Yes

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Gastroenteritis

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

Medical conditions at the time of the event included weight decrease.

On (b) (6), four months after the 2nd dose of flu quadrivalent split quebec, this 14-month-old subject developed gastroenteritis. The subject was hospitalised. The subject was treated with hydration therapy. The event resolved on 28 April 2011. The investigator considered that there was no reasonable possibility that the gastroenteritis may have been caused by Flu Quadrivalent split without adjuvant Quebec and that the event was possibly due to

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Prevnar 13
(Pneumococcal vac NonGSK)
MMR II vaccine
(MMR vaccine (Non-GSK))
Neisvac-C
(Meningococcal polysacchar)

(b) (6)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0015580B

24c. DATE RECEIVED: 26MAY2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0015580B	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

her medical condition of weight decrease.

Investigator Comments : Symptoms of vomiting and diarrhea started on 21Apr2011 and worsened on (b) (6) . Subject admitted to hospital on (b) (6) (x 1day). Symptoms improved on 25Apr2011 and resolved by 28Apr2011.
CONCOMITANT DRUGS AND DATES OF ADMINISTRATION

Varivax (b) (6)
(Varicella vir vacc nonGSK)

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
WEIGHT DECREASE	07Feb2010	Unknown	Yes

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Taiwan, ROC	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Bronchopneumonia, Hypovolaemia, Influenza

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-YB (Lot DFLUA039A).

On (b) (6), 81 days after the 1st dose of Blinded vaccine, this three-year-old subject developed influenza. On (b) (6), he developed bronchopneumonia and volume depletion. The subject was hospitalised. The subject was treated with oseltamivir phosphate, cyproheptadine, acetylcysteine, guaiphenesin, fenoterol, Augmentan, tipepidine hybenzate, ibuprofen, cefotaxime, lactic-acid-producing organisms, bromhexine, diclofenac, ceftibuten

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix YB Injection DFLUA039A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016157A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

and cetirizine hydrochloride. The volume depletion and influenza resolved on 15 February 2011. The bronchopneumonia resolved on 05 March 2011. The investigator considered that there was no reasonable possibility that the bronchopneumonia, volume depletion and influenza may have been caused by investigational product and that the events were possibly due to incidental illness.

Investigator Comments : This patient was sent to hospital in outpatient department on 2pm (b) (6) due to fever, severe productive cough, rhinorrhea, poor oral intake and activity, and decreased urine output, productive cough was since one week ago. According to clinical symptoms diagnosis influenza by doctor. Tamiflu was treated for 5 days. Then patient was admitted to emergency room on 10pm (b) (6) due to fever continue. The chest x-ray revealed increased density in retrocardiac left lung. He was admitted to ward on (b) (6) for medication treatment. The patient was discharged on (b) (6) in stable condition, and outpatient department follow up.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Blood CRP	(b) (6)	17.58mg/dL	0	0.8
Blood CRP		0.33mg/dL	0	0.8
Blood WBC		13.8910e3/ul	3.99	10.39
Blood WBC		6.7210e3/ul	3.99	10.39

INTERNATIONAL EVENT REPORT

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Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Foreign body

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

On (b) (6), 43 days after the 2nd dose of flu quadrivalent split quebec, this three-year-old subject was found to have a foreign body in esophagus. The subject was hospitalised. The event resolved on 15 January 2011. The investigator considered that there was no reasonable possibility that the foreign body in esophagus may have been caused by Flu Quadrivalent split without adjuvant Quebec.

Investigator Comments : March15/11 was notified of subject having a procedure in hospital. Upon further investigation, child was taken to Emergency Room (b) (6) with difficulty swallowing. An xray

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline — DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016401A

24c. DATE RECEIVED: 18MAR2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

(b) (6) showed a metalic oval density projected over the proximal esophagus. Subject was sent from St Joseph's ER to McMaster ER where a second Xray was done (b) (6) showing a 2cm opaque foreign object in the lower neck. Subject had swallowed a coin and it was stuck above the cricopharyngeus muscle in the upper esophagus. Subject was taken to Operating room where a penny was retrieved using optic forceps. There was no bleeding during the procedure, no tissue trauma, subject was taken to recovery and discharged a few hours later in good condition. Confirmed with mother Mar15/11 that no medications were administered. Confirmed with McMaster Mar15/11 that child was not admitted to hospital, ER procedure only.
Update on hospital admission. Subject was admitted to McMaster Pediatric OR.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Biliary dyskinesia, Vitello-intestinal duct remnant

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

Medical conditions at the time of the event included gastroesophageal reflux and ovarian cyst. Concomitant medications included Prilosec.

In October 2010, same month as the 1st dose of Blinded vaccine, this 17-year-old subject developed meckel diverticulum and biliary dyskinesia. The subject was hospitalised and the events were

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☒ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)

19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Omeprazole (b) (6)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016423A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

life-threatening. The subject was treated with Percocet, ondansetron hydrochloride, pantoprazole and ciprofloxacin hydrochloride. The events resolved on 08 March 2011. The investigator considered that there was no reasonable possibility that the biliary dyskinesia and meckel diverticulum may have been caused by investigational product and that the events were possibly due to the subject's medical conditions.

Investigator Comments : 16MAR2011 Office note discovered stating (b) (6) Call from mom stating that the subject is having outpatient removal of her gall bladder at UPMC Farrell today." Phone call made to parent to inquire about subject's condition. Per mom, subject ended up being admitted after the removal of her gallbladder due to an extended surgery that was exploratory in nature. Child was discharged in the evening of (b) (6) but was actually in the hospital for over 24 hours. Subject is in good condition now per mother. Phone call to surgeon's office requesting additional documentation pertaining to this surgery. 17MAR2011 Received surgeons records and updated RDE. On (b) (6) a nuclear medicine hepatobiliary scan without CCK impression: There is no evidence of complete obstruction of common or cystic bile ducts. Question increased visualization of intrahepatic ducts. A liver ultrasound is recommended in followup. On (b) (6) an ultrasound of the abdomen impression was: 1. Unremarkable gallbladder 2. Prominent pancreatic duct which is dilated to 4.5cm diameter. No choledocholithiasis is demonstrated.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
GASTROESOPHAGEAL REFLUX	01Jan2010	Unknown	Yes
OVARIAN CYST	27Nov2010	Unknown	Yes

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Asthma

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15 mcg HA/strain).

On (b) (6), 45 days after the 2nd dose of flu quadrivalent split quebec, this 26-month-old subject developed asthma. The subject was hospitalised. The subject was treated with ceftriaxone sodium, methylprednisolone sodium succinate, ibuprofen, paracetamol and salbutamol sulphate. The event resolved on 27 January 2011. The investigator considered that there was no reasonable possibility that the asthma may have been caused by Flu Quadrivalent split without adjuvant Quebec.

Relevant Risk Factors : Maternal uncle has history of asthma.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016446A

24c. DATE RECEIVED: 05AUG2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Investigator Comments : Patient is a 2 year-old, hispanic, male who was admitted on (b)(6) because of fever, coughing and difficullty of breathing for 3 days. Patient''s mother previously denied history of asthma. Upon admission, however, mother claimed that patient was diagnosed with asthma. Patient is still admitted as of this moment. Details of hospitalization and events leading to that are still pending. 2 year old male admitted from ER with symptoms as stated as above. During the course of hospitalization was given albuterol tabsm solu-medrol, steroids IV and antibiotics IV. Chest x-ray was normal. Symptoms improved and child was discharged home.

This case contains an event assessed by the investigator as a serious possible immune mediated disorder (pIMD).

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Blood Bands	(b) (6)	9%	0	9
Blood Basophils		0%	0	1
Blood Carbon dioxide		21%	22	30
Blood Eosinophils		0%	1	3
Blood Hematocrit		31.9%	42.0	52.0
Blood Hemoglobin		11.3g/dL	14.0	18.0
Blood Lymphocytes		9%	21	46
Blood Monocytes		1%	6	12
Blood Platelet count		418x10e3/mcL	130	400
Blood Red blood cell count		3.85x10e6/mcL	4.70	6.10
Blood Segmenters		81%	43	65
Blood WBC		13.1x10e3/mcL	4.8	10.8

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Gastroenteritis rotavirus

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-YB (Lot DFLUA039A).

On (b) (6), four months after the 2nd dose of Blinded vaccine, this four-year-old subject developed rotavirus. The subject was hospitalised. The subject was treated with paracetamol and ondansetron hydrochloride. The event resolved on 17 March 2011. The investigator considered that there was no reasonable possibility that the rotavirus may have been caused by investigational product.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix YB Injection DFLUA039A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016675A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0016675A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Investigator Comments : Medical records have been requested from hosptial. Day 180 phone call was completed on 28Mar2011. Per mother, subject was admitted into the hospital through the ER at St. Bernard's Hospital in Jonesboro Arkansas on (b) (6) and was discharged on (b) (6). Subject's vomiting and diarrhea started on (b) (6). Subject was admitted for more than 24 hours. On (b) (6), the following test were done : Basic Metabolic Panel, CBC, influenza A, influenza B, stool culture, urinalysis, and rotavirus. The rotavirus came back positive. Subject was given acetaminophen 270 mg on (b) (6) at 12:17 and was given ondansetron HCl 2.5 mg IV at 20:16. Patient was discharged on (b) (6). Subject was not given any medicines at discharge to take at home. Medical records have been obtained from the hospital and are filed in subject's source.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Stool Rotavirus	(b) (6)	POSITIVE		

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Spain	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Gastroenteritis

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

On (b) (6), 54 days after the 2nd dose of Blinded vaccine, this four-year-old subject developed acute gastroenteritis. The subject was hospitalised. The subject was treated with Glucosaline. The event resolved on 22 February 2011. The investigator considered that there was no reasonable possibility that the acute gastroenteritis may have been caused by investigational product.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)

19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Hepatitis A vaccine (b) (6)
(Hepatitis A vaccine)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016723A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Investigator Comments : Patient 4 years old came to his pediatrician on (b) (6) due to loose stools and vomiting since 5 days ago. She was diagnosed of acute gastroenteritis. She was hospitalized on (b) (6) for intravenous rehydration. Patient was discharged on (b) (6) in good condition.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Spain	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Accidental overdose

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6) she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

On (b) (6), 64 days after the 2nd dose of flu quadrivalent split quebec, this five-year-old subject developed accidental medication overdose (non-study). The subject was hospitalised. The event resolved on 02 March 2011. The investigator considered that there was no reasonable possibility that the accidental medication overdose (non-study) may have been caused by Flu Quadrivalent split without adjuvant Quebec.

Investigator Comments : Patient five months ago came to the emergency room on (b) (6) due to intake of 20 ml or 30 ml of

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016724A

24c. DATE RECEIVED: 08APR2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0016724A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

antihistamines. The patient was asymptomatic. She remains hospitalized fot 14hours without incident. The patient was dischanged on (b) (6) . She was in good condition.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Hypertension, Lymphadenitis

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

Concomitant medications included Trazodone hydrochloride, Focalin and Concerta.

On (b) (6), five months after the 1st dose of flu quadrivalent split quebec, this nine-year-old subject developed hypertension. On (b) (6), he developed mesenteric adenitis. The subject was hospitalised. The subject was treated with lisinopril, guanfacine hydrochloride, morphine, Norco, ibuprofen and dextrose. The mesenteric adenitis resolved on 24 March 2011. The hypertension resolved with sequelae on 24 March 2011. The investigator considered that there was no reasonable possibility that the

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Methylphenidate HCl
Focalin
(Dexmethylphenidate HCl)
Trazodone hydrochloride
(Trazodone hydrochloride)

(b) (6)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016818A

24c. DATE RECEIVED: 25AUG2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0016818A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

hypertension and mesenteric adenitis may have been caused by Flu Quadrivalent split without adjuvant Quebec.

Investigator Comments : On (b) (6) at 2:30am subject woke up with severe abdominal pain, vomiting, and fever. went to ER at 10:00am they did a CT and abdominal ultrasound they diagnosed subject with abdominal pain and constipation. On (b) (6) at 2:30am subject woke up again with abdominal pain and went back to ER. At that time they did another abdominal ultrasound and noticed swollen lymph nodes and subject was diagnosed with mesinteric adenitis with hypertension and was admitted to the hospital. Subject went home on (b) (6)

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Blood Creatine	(b) (6)	O.4mg/dL	0.6	1.3
Urine Mucous		PRESENT	ABSENT	
Urine Norepinephrine		186	27	110
Urine Rbc		0-2/hpf	ABSENT	

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Pneumonia viral, Asthma

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain).

On (b) (6), four months after the 2nd dose of flu quadrivalent split quebec, this three-year-old subject developed viral pneumonia.
On (b) (6), he developed asthma. The subject was hospitalised. The subject was treated with salbutamol sulphate, prednisolone sodium phosphate and fluticasone propionate. The events resolved on 20 April 2011. The investigator considered that there was no reasonable possibility that the viral pneumonia and asthma may have been caused by Flu Quadrivalent split without adjuvant Quebec.

Investigator Comments : Developed cough on 27Mar2011. Worsed with

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline DFLHA585A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016819A

24c. DATE RECEIVED: 23JUN2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0016819A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

difficulty breathing on 29Mar2011. Brought to Emergency dept on night of (b) (6) .
Diagnosed with asthma. Treated with Ventolin nebulizers and O2 35% and admitted to
hospital on (b) (6) . Started on daily dose of Pediapred. Continued Ventolin nebulizer
and O2. Chest xray showed patchy infiltration on left lower lobe and right middle lobe.
Possible viral pneumonia. Condition improved and was discharged home on (b) (6) on
Ventolin and Flovent inhalers.Pediaprel continued for a total of 5 daily doses.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Taiwan, ROC	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Pneumonia

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On 30 November 2010, she received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

On (b) (6) 116 days after the 1st dose of Blinded vaccine, this 17-year-old subject developed pneumonia. The subject was hospitalised. The subject was treated with ranitidine hydrochloride, phenoxymethylpenicillin potassium, acetylcysteine, azithromycin, cyproheptadine hydrochloride, ambroxol and Augmentin. The event resolved on 01 April 2011. The investigator considered that there was no reasonable possibility that the pneumonia may have

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)

19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016872A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0016872A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

been caused by investigational product and that the event was possibly due to incidental illness.

Investigator Comments : The patient was admitted to Emergency room due to severe chest pain at left chest with difficult breath on (b) (6) . The chest X-ray data (b) (6)): Blunting of left chest phase angle and increased density in left lower lung. Under the impression of left lower lung pneumonia, she was admitted to ward for antibiotic treatment, and steam inhalation were given. On (b) (6) , the chest X-ray data: Bilateral chest phase angles were sharp. Due to no fever and cough improve. The patient was discharged on (b) (6) and outpatient department follow up.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Blood C REACTIVE PROTEIN	(b) (6)	6.65mg/dL	0	0.8
Blood WHITE BLOOD COUNT		13.5910e3/ul	3.99	10.39

INTERNATIONAL EVENT REPORT

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Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Anaphylactic reaction, Urticaria, Hypersensitivity

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

Medical conditions at the time of the event included asthma, environmental allergy and prematurity.

On (b) (6), 103 days after the 2nd dose of Blinded vaccine, this four-year-old subject developed urticaria and anaphylactic reaction to food. On (b) (6), he developed a second episode

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☒ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016896A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

of urticaria and allergic reaction. The events were life-threatening. The subject was treated with diphenhydramine hydrochloride and dexamethasone. The anaphylactic reaction due to unspecified food resolved on 12 February 2011. The first episode of urticaria resolved on 17 February 2011. The second episode of urticaria and the allergic reaction resolved on 11 March 2011. The investigator considered that there was no reasonable possibility that the anaphylactic reaction to food, urticaria and allergic reaction may have been caused by investigational product and that the events were possibly due to the subject's medical conditions.

Investigator Comments : On (b) (6) subject taken to ER and diagnosed with urticaria and treated with IM Decadron and Benadryl. On (b) (6) subject again taken to ER and diagnosed with urticaria and allergic reaction and treated with IM Decadron and Benadryl. On (b) (6) subject seen by primary physician who considered ER events to be possible anaphylactic reactions and referred subject to an allergist for confirmation. Received specialist report on 13APR 2011 with confirmation of diagnosis of anaphylactic shock due to unspecified food. To clarify per query, ther first episode for the SAE was start date (b) (6) with a stop date of all symptoms on 17FEB2011. The second episode regarding the SAE was start date (b) (6) with stop date of 11MAR2011. Per ER report, chief complaint was: Hives, itchy throat. Exam showed: scattered hives on extremities and trunk, no respiratory distress, child was drinking pop when vitals were being taken.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
PREMATURITY	(b) (6)	Unknown	Yes
ASTHMA	2007	Unknown	Yes
ENVIRONMENTAL ALLERGY	2010	Unknown	Yes

INTERNATIONAL EVENT REPORT

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Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Suicidal ideation, Anxiety, Depression

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

Medical conditions at the time of the event included bipolar disorder, depression and post-traumatic stress disorder.

On (b) (6), 104 days after the 1st dose of Blinded vaccine, this 15-year-old subject developed suicidal ideation, depression-exacerbation and anxiety reaction. The events were life-threatening. On (b) (6), the suicidal ideation and

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☒ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)
GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0016913A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

anxiety reaction resolved. The depression-exacerbation was unresolved at time of reporting. The investigator considered that there was no reasonable possibility that the suicidal ideation, anxiety reaction and depression-exacerbation may have been caused by investigational product and that the events were possibly due to the subejct’s medical conditions.

Relevant Risk Factors : history of sexual abuse for 5 years, previous suicide attempt.

Investigator Comments : subject reportedly attempted suicide via drinking, records pending. Patient went to the emergeny department with suicidal ideation and suicide plan. Alcohol and recreation drug use tests negative. Patient on Prozac and Klonopin at the time of event, not related to event per PI. Suicidal ideation reported per records attempt not made.
Follow-up dated 31Aug2011 : request for medical records was made, no additional information has been provided.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
BIPOLAR DISORDER	2003	Unknown	Yes
DEPRESSION	Unknown	Unknown	Yes
POST-TRAUMATIC STRESS DISORDER	Unknown	Unknown	Yes

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Joint dislocation

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On 20 December 2010, he received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-YB (Lot DFLUA039A).

On (b) (6), five months after the 1st dose of Blinded vaccine, this 16-year-old subject experienced dislocated glenohumeral joint right side. The event was disabling. The subject was treated with anesthetic and ibuprofen. The event resolved on 15 June 2011. The investigator considered that there was no reasonable possibility that the dislocated glenohumeral joint right side may have been caused by investigational product.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☒ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix YB Injection DFLUA039A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)

19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0017928A

24c. DATE RECEIVED: 19SEP2011

DATE OF REPORT: 23SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0017928A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Investigator Comments : Subject dislocated right shoulder during a sports event on (b) (6) , subject taken to emergency same day. In emergency x-ray was done on right shoulder and diagnosis was dislocated glenohumeral joint. Subject was sedated and right shoulder was realigned. Subject left emergency after procedure wearing a clavicle splint brace on the (b) (6) . Subject is right handed and could not participate in any sports or P.E. classes in school. Subject took ibuprofen for pain from 28 May 2011 till 29 May 2011. On (b) (6) subject had another x-ray of right shoulder and Dr. visit. On (b) (6) subject visited Dr. and clavicle splint brace was removed, Dr stated x-ray showed right shoulder was healing well.

13.2.2. Pregnancy Case Narratives

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		F	Unknown

7. & 13. DESCRIBE EVENT(S)

Drug exposure before pregnancy

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

The subject's past medical history included no previous pregnancy. Father doesn't want to provide info on abnormal medical and family history.

Additional factor: Intake of Tetracycline 250 mg/cap Bid x 6 for ache started on 02 August 2010.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Intramuscular

17. NDICATION(S) FOR USE: Unknown

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Condom + spermicidal foam (Spermicide + Condom) Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0695785A

24c. DATE RECEIVED	DATE OF REPORT
19SEP2011	22SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

B0695785A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

On 21 January 2011, 3 months after the 1st dose of blinded vaccine, this 17-year-old subject was reported to be pregnant. Condom was used as contraception method. Her last menstrual period occurred on 30 November 2010. The subject was exposed to the vaccine before conception. On (b) (6), blood test was positive. The estimated delivery date was 07 September 2011.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Blood human chorionic gonadotropin	(b) (6)	142.000mIu/L		

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
PAIN	02Aug2010	Unknown	Unknown

13.2.3. Serious Adverse Events CIOMS (pIMDs)

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	United States	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Psoriasis

This male subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-YB (Lot DFLUA039A).

On (b) (6), 104 days after the 2nd dose of Blinded vaccine, this four-year-old subject developed psoriasis. The event was unresolved at time of reporting. The investigator considered that there was no reasonable possibility that the psoriasis may have been caused by investigational product.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix YB Injection DFLUA039A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Daptacel
(DTPa vaccine (Non-GSK))
MMR II vaccine
(MMR vaccine (Non-GSK))
Prevnar 13
(Pneumococcal vac NonGSK)

(b) (6)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0018059A

24c. DATE RECEIVED	DATE OF REPORT
19SEP2011	22SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0018059A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Investigator Comments : This a 4 year old male with a history of perrenial allergic rhinitis, eczema, otitis media, and a fractured right arm in the past. Parent brought subject for an allergy consult to the clinic on (b) (6) , who have possible reaction to food allergies (nuts and peanuts). All testing came out to be negative and it was diagnosed with Psoriasis.

This case contains an event assessed by the investigator as a non-serious possible immune mediated disorder (pIMD).
CONCOMITANT DRUGS AND DATES OF ADMINISTRATION

IPOL
(Polio vacc inact Non GSK)
Varivax
(Varicella vir vacc nonGSK)

(b) (6)

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 113314

Eudract No: 2010-021073-36

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT NITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Mexico	(b) (6)		F	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Vitiligo

This female subject was enrolled in the prophylactic study 113314 (FLU Q-QIV-003).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix -VB, identical to Fluarix with Victoria lineage B or Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Fluarix-VB (lot AFLUA521A).

On (b) (6), 120 days after the 2nd dose of Blinded vaccine, this seven-year-old subject was diagnosed with vitiligo. The subject was treated with betamethasone and tacrolimus. The event was unresolved at time of reporting. The investigator considered that there was no reasonable possibility that the vitiligo may have been caused by investigational product. The subject was withdrawn from the study

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PAT ENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ L FE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CL NICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENT F ED DRUG(S) Fluarix VB Injection AFLUA521A (INFLUENZA VIRUS VAC polyv)
GlaxoSmithKline

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Intramuscular

17. NDICATION(S) FOR USE: PROPHYLAXIS

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

14. DENT F ED DRUG(S)

20. D D EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION

17. NDICATION(S) FOR USE

21. D D EVENT REAPPEAR AFTER RE NTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

R0018357A

24c. DATE RECEIVED	DATE OF REPORT
21SEP2011	22SEP2011

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ INITIAL ☐ FOLLOW-UP

R0018357A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

due to the SAE.

Investigator Comments : On 22dec2010 the subject was included to the study and diagnosed as having an small hypochromic lesion on left malar region and leftt side of the neck, because was considered as dermatosis. During the study such lesions were growing in extension on the face and on (b) (6) after been evaluated by dermatologist the diagnosis was modified as vitiligo, which is a Mediated Immunological Disease. Before the subjet's inclusion and during the study the subject's mother covered up the lesions with make up which difficulted the diagnosis. On 17jun2011 the principal investigator and the study's medical staff analyzed the case and were agree with the clinical diagnosis of vitiligo. This report was not elaborated before because has been considered pre existent disease and currently after the diagnosis confirmed the subject must be excluded of the study. This case contains an event assessed by the investigator as a non-serious possible immune mediated disorder (pIMD).

GlaxoSmithKline Biologicals

Study title

Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) when administered in children.

Study detailed title

A Phase III, double-blind, randomised, controlled, multi-country, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to GSK Biologicals' trivalent influenza vaccine Fluarix™, administered intramuscularly to children 6 to 35 months of age.

Annex Report for Study 116926 (FLU Q-QIV-013)

Development Phase III

Indication Studied: Immunisation against influenza in male and female subjects 6 to 35 months of age inclusive.

Study initiation date:	01-November-2012
Study completion date:	19-June-2013
Data lock point (Date of database freeze):	17-September-2013
Date of report:	Final: 28-October-2013
Earlier Study Reports:	Clinical Study Report Flu Q-QIV-013 (Day 56), 06 June 2013 Clinical Study Report Flu Q-QIV-013 (Day 56) Amendment 1, 23 August 2013

Sponsor Signatory:	Varsha K. Jain, MD Director, Clinical Development Flu Vaccine GlaxoSmithKline Biologicals

This study was performed in compliance with Good Clinical Practice including the archiving of essential documents.

GSK Biologicals' Study Report INS-BIO-CLIN-1010 v04

SYNOPSIS

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium** **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured **Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1 pdm09), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(for national authority only)**

Study No.: 116926 (FLU Q-QIV-013)

Title of the study: A Phase III, double-blind, randomised, controlled, multi-country, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to GSK Biologicals' trivalent influenza vaccine *Fluarix*, administered intramuscularly to children 6 to 35 months of age.

Rationale for the Annex Report:
This Annex Report presents the safety analyses of the FLU Q-QIV and *Fluarix* vaccines in terms of medically attended adverse events (MAEs), serious adverse events (SAEs), and potential immune-mediated diseases (pIMDs) follow-up data collected from Day 0 up to the Day 180 phone contact (last time point in the study).

Principal investigators:
This study was conducted by eight investigators in three countries (Canada, Dominican Republic and Honduras).

Study Centres:
Multi-centre study with six centres in Canada, one centre in Dominican Republic and one centre in Honduras.

Publication (reference): Not published as of 28-October-2013

Study period: **Study initiation date:** 01-November-2012 **Study completion date:** 19-June-2013 **Data lock point (Date of database freeze):** 17-September-2013	**Phase: III**

Indication: Immunisation against influenza in male and female subjects 6 to 35 months of age inclusive.

Treatment:
The study groups were as follows:

- Q-QIV: subjects received one dose (primed* subjects) of the FLU Q-QIV vaccine on Day 0 or two doses (unprimed** subjects) on Day 0 and Day 28
- D-TIV-YB: subjects received one dose (primed* subjects) of *Fluarix* on Day 0 or two doses (unprimed** subjects) on Day 0 and Day 28

*Primed subjects received two doses of a seasonal influenza vaccine separated by at least one month during the last season or at least one dose prior to the last season.
**Unprimed subjects did not receive any seasonal influenza vaccine in the past or only one dose for the first time in the last influenza season.

Objectives (pertaining to this Annex Report):
Secondary:

- To describe the safety of FLU Q-QIV and *Fluarix* in terms of:
  - SAEs, MAEs, and pIMDs during the entire study period.

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium** **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured **Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1 pdm09), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(for national authority only)**

Study design:
This was a Phase III, double-blind, randomised (1:1), controlled study with two parallel study groups to evaluate the immunogenicity and reactogenicity of FLU Q-QIV in children 6 to 35 months of age. Blood samples were collected on Day 0 and Day 28 for primed subjects and on Day 0 and Day 56 for unprimed subjects.

Study vaccine, dose, mode of administration, lot no.:
Vaccination schedule /site:
One or two intramuscular (IM) injection(s) in the anterolateral side of left thigh (subjects < 12 months of age) or in the deltoid muscle of the non-dominant arm (subjects ≥ 12 months of age) on Day 0 (primed subjects) or Day 0 and Day 28 (unprimed subjects).

Vaccine composition /dose /lot number:
The quadrivalent influenza virus (FLU Q-QIV) candidate vaccine contained haemagglutinin (HA) from four influenza strains with a total of 60 µg (15 µg for each strain): A/California/7/2009 (H1N1 pdm09), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Hubei-Wujiagang/158/09 (Yamagata lineage). The formulation was thimerosal-free. The total volume injected was 0.5 mL. The lot number was DFLHA760A.

Reference vaccine /Comparator, dose and mode of administration, lot no.:
Vaccination schedule /site:
One or two IM injection(s) in the anterolateral side of left thigh (subjects < 12 months of age) or in the deltoid muscle of the non-dominant arm (subjects ≥ 12 months of age) on Day 0 (primed subjects) or Day 0 and Day 28 (unprimed subjects).

Vaccine composition /dose /lot number:

The trivalent control vaccine (D-TIV-YB), commercially available as *Fluarix*, contained HA from three influenza strains with a total of 45 µg (15µg for each strain): A/California/7/2009 (H1N1 pdm09), A/Victoria/361/2011 (H3N2), and B/Hubei-Wujiagang/158/09 (Yamagata lineage). The formulation was thimerosal-free. The total volume injected was 0.5 mL. The lot number was AFLUA726A.

Study Population:
Healthy male or female infants between, and including, 6 and 35 months of age at the time of the first vaccination, without prior receipt of any seasonal or pandemic influenza vaccine within six months preceding the first dose of the study vaccine, or planned use during the study period, for whom the investigator believed that their parents/legally acceptable representatives (LARs) would comply with the requirements of the protocol. Written informed consent was obtained from the parents/LARs of each subject.

Duration of treatment:
The duration of the study was approximately 3 to 5 weeks to complete enrolment and approximately 6 months for each enrolled subject to complete the study.

Secondary Outcome/Efficacy Variable(s) (pertaining to this Annex Report):
- SAEs, MAEs, and pIMDs:
  - Occurrence of SAEs, MAEs and pIMDs (summarised by incidence rate and relationship to vaccination) during the entire study period.

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium** **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured **Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1 pdm09), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(for national authority only)**

Statistical methods (pertaining to this Annex Report):
The statistical analyses were performed as per protocol and per Statistical Analysis Plan (SAP).

Safety:

The analysis of safety was performed on the Total Vaccinated cohort (TVC) (primary analysis).

- The percentage of subjects reporting AEs resulting in a medically attended visit was tabulated with exact 95% confidence interval (CI) for the entire study period (up to the Day 180 phone contact).
- SAEs and pIMDs were collected and summarised for the entire study period.

Synopsis Table 1: Study population (Total Vaccinated cohort)

Number of subjects	Q-QIV	D-TIV-YB	Total
N (Total Vaccinated cohort)	299	302	601
Completed, n	287	294	581
Withdrawn	12	8	20

Q-QIV = FLU Q-QIV vaccine; D-TIV-YB = *Fluarix* vaccine; N = total number of subjects; n = number of subjects

Summary:

This Annex Report describes the analysis which was performed when data on safety endpoints were obtained up to and including Day 180.

Safety:

The safety analysis was performed on the TVC (primary analysis).

Medically attended adverse events:

- Overall, at least one unsolicited MAE up to the Day 180 phone contact was reported for 156 (52.2%) and 156 (51.7%) subjects in the Q-QIV group and D-TIV-YB group, respectively. Nasopharyngitis (27.1% and 25.5% of subjects, respectively), diarrhoea (8.0% and 9.6% of subjects, respectively) and pharyngitis (5.7% and 2.6% of subjects, respectively) were the only unsolicited MAEs reported by more than 5.0% of subjects in any study group.

Serious adverse events:

- During the entire study period, a total of 25 non-fatal SAEs were reported for 17 subjects. SAEs were reported for nine (3.0%) and eight (2.6%) subjects in the Q-QIV group and D-TIV-YB group, respectively. One of the SAEs reported in the Q-QIV group at the day of the vaccination (febrile convulsion) was considered by the investigator as related to the study vaccination, and resolved on the same day. This febrile convulsion case was initially reported as an AE in the main study report (Day 56). It was upgraded to an SAE by the investigator at GSK's request because febrile convulsion is considered a potential risk under close monitoring. Therefore, this case is reported as an SAE in this Annex Report. All reported SAEs resolved by the end of the study (Day 180 phone contact). No fatal SAEs were reported.

Withdrawals due to adverse events /serious adverse events:

- No subject withdrew due to an AE or SAE from Day 0 up to the Day 180 phone contact.

Other safety parameters:

- During the entire study period, no pIMDs were reported for the subjects in the Q-QIV group. Two cases of pIMDs (alopecia areata and colitis ulcerative) were reported in the D-TIV-YB group. All reported pIMDs resolved by the end of the study (Day 180 phone contact).

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium** **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured **Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1 pdm09), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(for national authority only)**

Conclusion:

- At least one unsolicited MAE was reported for 156 (52.2%) and 156 (51.7%) subjects in the Q-QIV group and D-TIV-YB group, respectively. Nasopharyngitis (27.1% and 25.5% of subjects, respectively), diarrhoea (8.0% and 9.6% of subjects, respectively) and pharyngitis (5.7% and 2.6% of subjects, respectively) were the only MAEs reported by more than 5.0% of subjects in any study group.
- SAEs were reported for nine (3.0%) and eight (2.6%) subjects in the Q-QIV group and D-TIV-YB group, respectively. One of the SAEs reported in the Q-QIV group at the day of the vaccination (febrile convulsion) was considered by the investigator as related to the study vaccination, and resolved on the same day. No fatal SAEs were reported.
- Two cases of pIMDs (alopecia areata and colitis ulcerative) were reported, both in the D-TIV-YB group.

Date of report: Final: 28-October-2013

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LIST OF ABBREVIATIONS

AE	Adverse Event
ATP	According-to-Protocol
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CIOMS	Council for International Organisations of Medical Sciences
CRDL	Clinical Research & Development Lead
CRF	Case Report Form
CRO	Contract Research Organisation
CSR	Clinical Study Report
eCRF	electronic Case Report Form
GCP	Good Clinical Practice
GSK	GlaxoSmithKline
HA	Haemagglutinin
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IM	Intramuscular
IRB	Institutional Review Board
LAR	Legally Acceptable Representative
LL	Lower Limit
MAE	Medically Attended Adverse Events
MedDRA	Medical Dictionary for Regulatory Activities
NACI	National Advisory Committee on Immunization
pIMD	potential Immune-Mediated Disease
PT	Preferred Term
QIV	Quadrivalent
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SBIR	Randomisation System on Internet

SOPs	Standard Operating Procedures
SPM	Study Procedures Manual
TIV	Trivalent
TVC	Total Vaccinated cohort
UL	Upper Limit
WHO	World Health Organisation
WRC	Worldwide Regulatory Compliance

GLOSSARY OF TERMS

Adverse event (AE): Any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An adverse event (AE) was therefore any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this included failure to produce expected benefits (i.e., lack of efficacy), abuse or misuse.

Blinding: A procedure in which one or more parties to the trial are kept unaware of the treatment assignment in order to reduce the risk of biased study outcomes. The level of blinding is maintained throughout the conduct of the trial, and only when the data are cleaned to an acceptable level of quality will appropriate personnel be unblinded or when required in case of a serious adverse event (SAE). In a double blind study, the subject, the investigator and sponsor staff who are involved in the treatment or clinical evaluation of the subjects and the review or analysis of data are all unaware of the treatment assignment.

Child in care: A child who has been placed under the control or protection of an agency, organisation, institution or entity by the courts, the government or a government body, acting in accordance with powers conferred on them by law or regulation. The definition of a child in care can include a child cared for by foster parents or living in a care home or institution, provided that the arrangement falls within the definition above. The definition of a child in care does not include a child who is adopted or has an appointed legal guardian.

Eligible: Qualified for enrolment into the study based upon strict adherence to inclusion/exclusion criteria.

Epoch: An epoch is a self-contained set of consecutive time points or a single time point from a single protocol. Self-contained means that data collected for all subjects at all time points within that epoch allows to draw a complete conclusion to define or precise the targeted label of the product. Typical examples of epochs are primary vaccinations, boosters, yearly immunogenicity follow-ups, and surveillance periods for efficacy or safety.

eTrack:	GlaxoSmithKline (GSK)'s tracking tool for clinical trials.
Evaluable:	Meeting all eligibility criteria, complying with the procedures defined in the protocol, and, therefore, included in the according-to-protocol (ATP) analysis (see Sections 5.6 and 5.10.3 for details on criteria for evaluability).
Investigational vaccine/product: **(Synonym of Investigational Medicinal Product)**	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Potential Immune-Mediated Disease (pIMDs):	Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.
Primed subjects:	All subjects who have received two doses of seasonal influenza vaccine separated by at least one month during the last season or have received at least one dose prior to last season.
Randomisation:	The process of assigning trial subjects to study material pertaining to groups using an element of chance to determine the assignments in order to reduce bias.
Self-contained study:	Study with objectives not linked to the data of another study.
Serious Adverse Event (SAE):	Any untoward medical occurrence in a patient or clinical investigation subject that: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.
Solicited AE:	AEs to be recorded as endpoints in the clinical study. The presence/occurrence/intensity of these events is actively solicited from the subject or an observer during a specified post-vaccination follow-up period.
Subject:	Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the clinical study, either as a recipient of the vaccine(s)/product(s) or as a control.
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the study.

Treatment:	Term used throughout the clinical study to denote a set of investigational product(s) or marketed product(s) or placebo intended to be administered to a subject, identified by a unique number, according to the study randomisation or treatment allocation.
Unprimed subjects:	Subjects who have not received any seasonal influenza vaccine in the past or received only one dose for the first time in the last influenza season.
Unsolicited AE:	Any AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited AE.

TRADEMARKS

The following trademarks are used in the present Annex Report.

Note: In the body of the Annex Report (including the synopsis), the names of the vaccines/products and/or medications will be written without the superscript symbol ™ or ® and in *italics*.

Trademarks of the GlaxoSmithKline group of companies	Generic description
Fluarix™	Inactivated trivalent split virion influenza vaccine

1. ETHICS

1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational centre Independent Ethics Committee (IEC) and Institutional Review Board (IRB).

1.2. Ethical conduct of the study

Overall, this study was conducted in accordance with "good clinical practice" (GCP) and all applicable regulatory requirements, including the Declaration of Helsinki.

During the course of the study, whenever potential issues with regard to the conduct of the study were identified, either via site monitoring activities or brought to GlaxoSmithKline (GSK) Biologicals' attention by other oversight mechanisms, these issues were investigated and appropriate corrective and/or preventive actions where possible were taken. Refer to Sections 5.11 and 6.2.3.

1.3. Subject information and consent

Written informed consent was obtained from each parent/Legally Acceptable Representative (LAR) prior to the performance of any study-specific procedures. Case report forms (CRFs) were provided for each subject's data to be recorded.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

2.1. Administrative structure

This study was conducted by eight investigators in three countries (Canada, Dominican Republic and Honduras).

GSK Biologicals was responsible for administration of the study, including clinical trial supply management and laboratory facilities for immunological testing.

Data management was performed by Keyrus, contractor for GSK Biologicals, Lasne, Belgium. Statistical analyses were performed by GSK Biologicals. Writing of the study protocol and clinical study report (CSR) was performed by Emtex, contractor for GSK Biologicals, Sint-Gillis-Waas, Belgium. Monitoring at the sites was performed by GSK Inc. Canada, Arka Servicios de Recursos Humanos S.A., Panama and GSK Panama.

2.2. Clinical Study Report revision history

The main study report (Day 56) was amended; for detailed information, refer to the FLU--Q-QIV-013 (Day 56) Amendment 1 study report dated 23 August 2013.

3. INTRODUCTION

Influenza is a serious public health problem; it has a high incidence in the human population and causes regular large-scale morbidity and mortality. During seasonal epidemics, 5-15% of the worldwide population is typically infected, resulting in 3-5 million cases of severe illness and a quarter to half a million excess deaths annually. Most deaths associated with influenza in industrialised countries occur among people 65 years of age or older [WHO, 2009], although infection is most common in children [O'Brien, 2004; Izurieta, 2000]. In particular, children younger than 5 years of age have incidence rates of severe influenza disease and hospitalisation due to influenza second only to the elderly population.

The highest influenza burden in terms of paediatric respiratory admissions is seen in infants 6 to 11 months of age [Schanzer, 2006] and rates of illness in children younger than 2 years of age are substantially higher than those in children 2 years of age or older [CDC, 2007; Poehling, 2006]. Children also play an important role in the spread of the disease [Brownstein, 2008], possibly because of their high levels of virus shedding. Since annual influenza vaccination is currently the most effective means of controlling influenza and preventing its complications and mortality [WHO, 2009], there is a general trend to extend the recommendation for influenza vaccinations not only to children at high risk of complicated influenza, but also to healthy children and adolescents. The effectiveness of influenza vaccination is, however, dependent on adequate matching between the circulating viruses and the viruses contained in the vaccine, the age of the child and the type of vaccine.

Since 1983, two antigenically distinct lineages of influenza B have circulated in the world. Their co-existence has also resulted in the emergence and subsequent worldwide circulation of a reassortant B virus possessing a Victoria-lineage haemagglutinin (HA) with a Yamagata-lineage derived neuraminidase [Barr, 2006]. In the United States, both Yamagata and Victoria lineages have co-circulated since the 2001-2002 influenza season.

Sera from adults vaccinated with the virus from one B lineage show some modest level of cross-reactivity against the other B lineage *in vitro*, which may be due to a prior natural exposure or vaccine priming [Barr, 2006; Heckler, 2007]. However, infants and children are much less likely to generate such a cross-reactive antibody response, presumably because of limited prior immunologic experience with influenza, and thus may be more susceptible than adults to infection with a co-circulating alternate lineage B strain. In studies of unimmunised (unprimed) infants, no measurable cross-reactive antibodies to the alternate B lineage were found in the sera of naïve children after their first vaccine exposures [Hannoun, 2004; Heckler, 2007; Hobson, 1972]. Englund also showed that young children who have been exposed to prior priming manifested good boosting of influenza A responses, even when the vaccine virus has drifted somewhat from the original priming exposure. However, cross-lineage B virus priming was quite poor [Englund, 2006]. Sera from naïve ferrets (modelling young children) that are infected with a single B virus (and not exposed to other human influenza viruses), also show little or no cross-reactivity between the two B lineages [Barr, 2006].

From 2001 to 2009, influenza B viruses have accounted for 6.9% to 38.7% of clinical isolates from Centers for Disease Control (CDC) surveillance [CDC, 2010]. In 5 of these 8 years, a substantial proportion of B virus isolates have been representative of the

genetic lineage not included in the trivalent (TIV) vaccine, and have accounted for 6.4% to 29.9% (median of 8.5%) of all influenza virus isolates [CDC, 2010].

The consequences of such a B virus mismatch could be severe. During the 2007-2008 season, almost 30% of influenza viruses tested at the CDC in the United States were type B, and 98% of them did not match the lineage contained in the TIV vaccine [CDC, 2008]. Assuming that a quadrivalent (QIV) vaccine containing a second B strain had been used in the 2007-2008 season rather than a TIV vaccine, a public health impact model for influenza-associated health outcomes estimated that the QIV seasonal vaccine could have prevented an additional 1090514 influenza cases, and resulted in 7488 fewer hospitalisations and 321 fewer deaths [Reed, 2009]. Because the two evolutionarily distinct lineages of influenza B virus continue to co-circulate, and cross-reactivity between the two lineages is low in the paediatric population (which has limited immunologic experience with influenza), an additional B strain antigen in the seasonal vaccine may offer greater efficacy and broader protection to children [Englund, 2006; Levandowski, 1991]. In addition, the 2007-2008 experience suggested that mismatched B virus morbidity was substantial in the elderly [Proff, 2009]; and these vulnerable persons could theoretically benefit from improved herd immunity resulting from immunisation of children as well as direct immunisation. These considerations have lead GSK Biologicals to develop a candidate QIV seasonal influenza vaccine, FLU Q-QIV (GSK2282512A), comprised of two A and two B strains.

Fluarix, formulated with two influenza A strains (A/H1N1 and A/H3N2) and one influenza B strain (Yamagata lineage B strain), is licensed for use in children 6 months of age and older in many countries. The Yamagata lineage B strain in *Fluarix* is the B strain recommended by the World Health Organisation (WHO) for the Northern Hemisphere 2012-2013 influenza season. The QIV vaccine, termed Q-QIV to indicate that it is manufactured at the Quebec site, is formulated with two influenza A strains (A/H1N1 and A/H3N2) and two influenza B strains (the same Yamagata lineage B strain as that in *Fluarix*, as well as a second Victoria lineage, B strain).

FLU Q-QIV has been studied in 300 children 6 to 35 months of age, given as a 0.5 mL dose in an open arm of the paediatric study, FLU Q-QIV-003. The 0.5 mL dose was well tolerated and immunogenic in children 6 to 35 months of age in this study, however no control vaccine was used. The primary purpose of this FLU Q-QIV-013 study was to evaluate the immunogenicity and reactogenicity of Q-QIV with respect to a TIV control, *Fluarix,* in children 6 to 35 months of age.

4. STUDY OBJECTIVES

The objective mentioned below is specific to the analyses presented in this Annex Report. All other objectives of the study were described in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report.

4.1. Secondary objective

- To describe the safety of FLU Q-QIV and *Fluarix* in terms of:
  - Serious adverse events (SAEs), medically attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period.

See Section 5.10.1 for details of the study endpoints pertaining to this Annex Report.

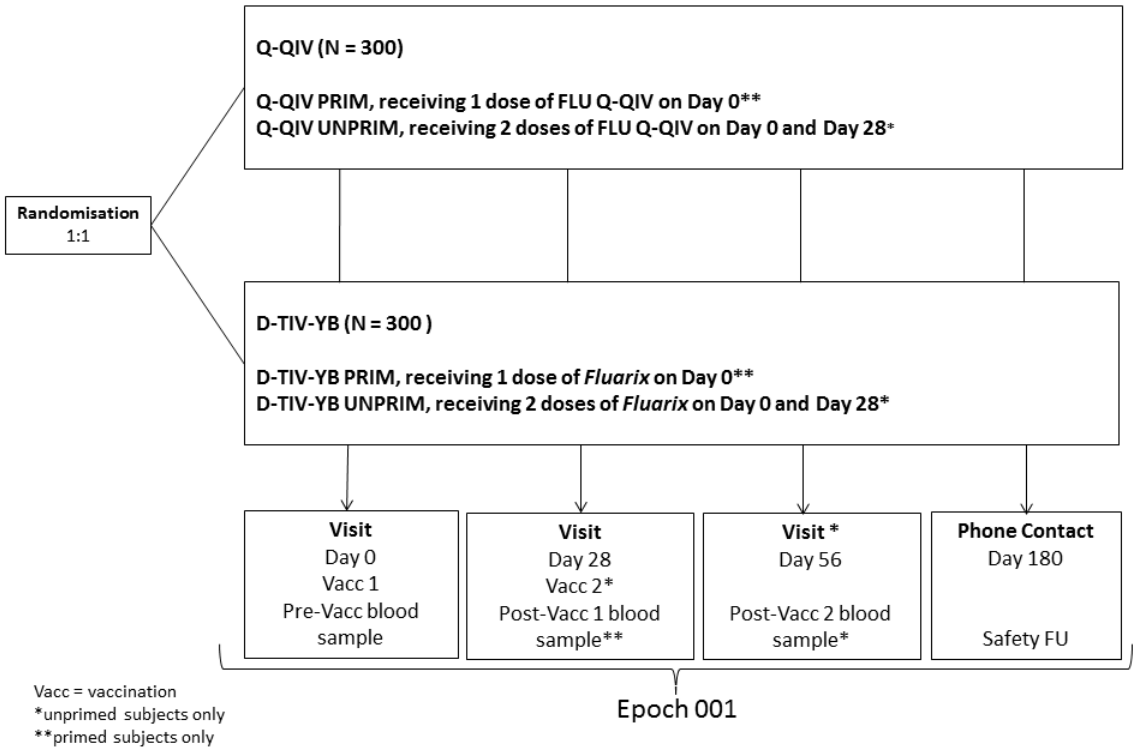
5. INVESTIGATIONAL PLAN

5.1. Study design

5.1.1. Overall study design – Description

Figure 1 provides a schematic overview of the study design.

Figure 1 Study design



- **Experimental design:** Phase III, double-blind, randomised, controlled, parallel-group, multi-centre, and multi-country study.
- **Duration of the study:** Approximately 3 to 5 weeks to complete enrolment and approximately 6 months for each enrolled subject to complete the study.
  - Epoch 001: Primary starting at Visit Day 0 and ending at Phone Contact Day 180.

- **Study groups:**

Table 1 Study groups and epochs foreseen in the study

Study Groups	Number of subjects	Age (Min – Max) (age unit)	Epochs
			Epoch 001
Q-QIV PRIM	300	6 months - 35 months	x
Q-QIV UNPRIM			
D-TIV-YB PRIM	300	6 months - 35 months	x
D-TIV-YB UNPRIM			

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine name	Study Groups			
		Q-QIV PRIM	Q-QIV UNPRIM	D-TIV-YB PRIM	D-TIV-YB UNPRIM
Q-QIV	FLU Q-QIV	x	x		
D-TIV-YB	*Fluarix*			x	x

- **Control:** active control (*Fluarix*)
- **Vaccination schedules:**
  - Primed* subjects (Q-QIV PRIM and D-TIV-YB PRIM): one intramuscular (IM) injection, on Day 0.
  - Unprimed* subjects (Q-QIV UNPRIM and D-TIV-YB UNPRIM): two IM injections, on Day 0 and Day 28.

  *See GLOSSARY OF TERMS for definitions of primed and unprimed subjects.
- **Treatment allocation**: Subjects were randomised 1:1 in the Q-QIV and D-TIV-YB groups.
  - Age (6 to 17 months, 18 to 35 months), study centre and the pre-study influenza priming status of the subjects were treated as minimisation factors to ensure equal representation of primed versus unprimed subjects, as well as equal representation of different age groups, and different centres in the two treatment groups.
- **Blinding**:

Table 3 Blinding of study epochs

Study Epochs	Blinding
Epoch 001	double-blind

Refer to Section 5.5 for details of unblinding.

- **Sampling schedule**: Blood samples were collected on Day 0 and Day 28 for primed subjects and on Day 0 and Day 56 for unprimed subjects.
- **Type of study**: self-contained
- **Data collection**: electronic Case Report Form (eCRF)

5.1.2. Discussion of study design

This study was intended to generate controlled data of the FLU Q-QIV candidate vaccine in children 6 to 35 months of age. In particular, this study was designed to estimate the expected incidence of solicited AEs following administration of FLU Q-QIV in contrast to a licensed D-TIV (*Fluarix*) vaccine. Fever following vaccination was an objective measure of reactogenicity that was solicited. As fever following vaccination could be associated with febrile convulsions in this age group, the study's sample size was designed to afford a high probability to detect fever ≥ 38°C or fever ≥ 39°C. The group size (N = 300 per treatment) also permitted an exploratory subgroup analysis of responses by age (6 to 17 months, 18 to 35 months).

Moreover, the sample size in this study when combined with supportive data from other completed controlled and uncontrolled studies of GSK's QIV formulations created a safety database of approximately 1000 subjects 6 to 35 months of age.

The control vaccine was *Fluarix* (D-TIV), which is licensed for use in children 6 months of age and older in many countries.

Unprimed study participants received two 0.5 mL doses of FLU Q-QIV or *Fluarix* were administered IM at an approximate 28-day interval. Primed subjects received a single 0.5 mL dose of FLU Q-QIV or *Fluarix*. The 0.5 mL dose has been routinely recommended by the National Advisory Committee on Immunization (NACI) for children 6 to 35 months of age for inactivated seasonal flu vaccines since 2011.

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information on immunogenicity.

5.2. Study procedures

5.2.1. Outline of study procedures

Table 4 and Table 5 summarise the list of study procedures during study visits and the final study contact for primed and unprimed subjects, respectively.

Table 4 List of study procedures for primed subjects – one vaccine dose

Age	6 to 35 months		
Epoch	Epoch 001		
Type of contact	visit	visit	phone contact
Time points	Day 0	Day 28	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	
Informed consent by parent(s)/LAR(s)	●		
Check inclusion/exclusion criteria	●		
Check elimination criteria)		●	●
Check contraindications to vaccination	●		
Collect demographic data (including weight and height)	●		
Medical history	●		
History of influenza vaccination	●		
Physical examination (history directed)	●	O §	
Pre-vaccination body temperature	●		
Internet randomisation	●		
Blood sampling (approximately 4 mL) for humoral immune response determination	●	●	
Vaccine administration	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily* (Days 0-6) and unsolicited AEs (Days 0-27)	O		
Return of diary cards		O	
Diary card transcription by investigator		●	
Record any concomitant medication/vaccination	●	●	●
Record any intercurrent medical conditions **	●	●	●
Recording of SAEs	● #	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●
Recording of MAEs and pIMDs	●	●	●
Study conclusion			●

LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; pIMDs = potential Immune-Mediated Diseases; SAE = Serious Adverse Event; Vacc = vaccination

● used to indicate a study procedure that required documentation in the individual eCRF.

○ used to indicate a study procedure that did not require documentation in the individual eCRF.

§ if deemed necessary by the investigator.

* Parent(s)/LAR(s) were instructed to immediately report any convulsion (seizure) or fever ≥ 39.0°C (102.2˚F) within two days of vaccination (i.e., day of vaccination and following day).

** These were conditions which could impact the immune response.

Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

Table 5 List of study procedures for unprimed subjects – two vaccine doses

Age	6 to 35 months			
Epoch	Epoch 001			
Type of contact	visit	visit	visit	phone contact
Time points	Day 0	Day 28	Day 56	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	Post-Vacc 2	
Informed consent by parent(s)/LAR(s)	●			
Check inclusion/exclusion criteria	●			
Check elimination criteria		●	●	●
Check contraindications to vaccination	●	●		
Collect demographic data (including weight and height)	●			
Medical history	●			
History of influenza vaccination	●			
Physical examination (history directed)	●	O §	O §	
Pre-vaccination body temperature	●	●		
Internet randomisation	●			
Blood sampling (approximately 4 mL) for humoral immune response determination	●		●	
Vaccine administration	●	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily* (Days 0-6) and unsolicited AEs (Days 0-27)	O	O		
Return of diary cards		O	O	
Diary card transcription by investigator		●	●	
Record any concomitant medication/vaccination	●	●	●	●
Record any intercurrent medical conditions **	●	●	●	●
Recording of SAEs	● #	●	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●	●
Recording of MAEs and pIMDs	●	●	●	●
Study conclusion				●

LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; pIMDs = potential Immune-Mediated Diseases; SAE = Serious Adverse Event; Vacc = vaccination

● used to indicate a study procedure that required documentation in the individual eCRF.

○ used to indicate a study procedure that did not require documentation in the individual eCRF.

§ if deemed necessary by the investigator.

* Parent(s)/LAR(s) were instructed to immediately report any convulsion (seizure) or fever ≥ 39.0°C (102.2˚F) within two days of vaccination (i.e., day of vaccination and following day).

** These were conditions which could impact the immune response

Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

5.2.2. Intervals between study visits

The time intervals between study visits of participants are presented in Table 6.

Table 6 Intervals between study visits

Interval	Optimal length of interval [1]	Allowed interval
Day 0 → Day 28	28 days	25 - 42 days
Day 28 → Day 56 *	28 days	25 - 42 days
Day 0 → Day 180	180 days	166 -201 days

[1] Whenever possible the investigator had to arrange study visits within this interval.
*Only applicable for unprimed subjects.

5.3. Selection of study population

This study was conducted at multiple sites in three countries (Canada, Dominican Republic and Honduras). Enrolment was terminated when approximately 600 subjects were randomised and dosed.

5.3.1. Inclusion criteria for enrolment

All subjects had to satisfy ALL the following criteria at study entry:

- Subject's parent(s)/LAR(s) who, in the opinion of the investigator, could and would comply with the requirements of the protocol (e.g., completion of the diary cards, return for follow-up visits).
- A male or female between, and including, 6 and 35 months of age at the time of the first vaccination.
- Written informed consent obtained from the parent(s)/LAR(s) of the subject.
- Subjects in stable health as determined by investigator's clinical examination and assessment of subject's medical history.
- Subjects were eligible regardless of history of administration of influenza vaccine in a previous season.

5.3.2. Exclusion criteria

The following criteria were to be checked at the time of study entry. If ANY exclusion criterion applied, the subject was not included in the study:

- Use of any investigational or non-registered product (drug or vaccine) other than the study vaccine within 30 days preceding the first dose of study vaccine, or planned use during the study period. Routine registered childhood vaccinations were permitted.
- Child in care

  Please refer to the GLOSSARY OF TERMS for the definition of child in care.
- Prior receipt of any seasonal or pandemic influenza vaccine (registered or investigational) within six months preceding the first dose of study vaccine, or planned use during the study period.

- Chronic administration (defined as more than 14 days in total) of immunosuppressants or other immune-modifying drugs within six months prior to the first vaccine dose. For corticosteroids, this meant prednisone ≥ 0.5 mg/kg/day, or equivalent. Inhaled and topical steroids were allowed.
- Administration of immunoglobulins and/or any blood products within the three months preceding the first dose of study vaccine or planned administration during the study period.
- History of Guillain-Barré syndrome within 6 weeks of receipt of prior influenza vaccine.
- Any known or suspected allergy to any constituent of influenza vaccines (including egg proteins); a history of anaphylactic-type reaction to consumption of eggs; or a history of severe adverse reaction to a previous influenza vaccine.
- Acute disease and/or fever at the time of enrolment.
  - Fever was defined as temperature ≥ 38.0°C/100.4°F by any method.
  - Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever could be enrolled at the discretion of the investigator.
- Any significant disorder of coagulation or treatment with warfarin derivatives or heparin.
- Any confirmed or suspected immunosuppressive or immunodeficient condition, based on medical history and physical examination (no laboratory testing required).
- Any other condition which, in the opinion of the investigator, prevented the subject from participating in the study.

5.3.3. Elimination criteria

The use of the following concomitant medications/products/vaccines did not require withdrawal of the subject from the study but could determine a subject's evaluability in the according-to-protocol (ATP) analysis. See Section 5.10.3 for study cohorts/data sets analysed.

- Any investigational or non-registered product (drug or vaccine) other than the study vaccine(s) used during the study period.
- Immunosuppressants or other immune-modifying drugs administered chronically (i.e., more than 14 days) during the study period. For corticosteroids, this meant prednisone ≥ 0.5 mg/kg/day, or equivalent. Inhaled and topical steroids were allowed.
- Administration of influenza vaccines other than the study vaccines during the study period.
- Immunoglobulins and/or any blood products administered during the study period.

At each study visit subsequent to the first vaccination visit, it had to be verified if the subject experienced or was experiencing any intercurrent medical condition. If it was the case, the condition(s) had to be recorded in the eCRF.

Subjects could be eliminated from the ATP cohort for immunogenicity if, during the study, they incurred a condition that had the capability of altering their immune response, i.e., any confirmed or suspected immunosuppressive or immunodeficient condition, based on medical history and physical examination (no laboratory testing required).

5.3.4. Subject completion and withdrawal

5.3.4.1. Subject completion

A subject who returned for the concluding visit/was available for the concluding contact foreseen in the protocol was considered to have completed the study.

5.3.4.2. Subject withdrawal

Subjects who were withdrawn because of SAEs/AEs had to be clearly distinguished from subjects who were withdrawn for other reasons. Investigators followed subjects who were withdrawn as result of an SAE/AE until resolution of the event.

Withdrawals were not replaced.

5.3.4.2.1. Subject withdrawal from the study

From an analysis perspective, a 'withdrawal' from the study referred to any subject who did not come back for the concluding visit/was not available for the concluding contact foreseen in the protocol.

All data collected until the date of withdrawal/last contact of the subject were used for the analysis.

A subject was considered a 'withdrawal' from the study when no study procedure had occurred, no follow-up had been performed and no further information had been collected for this subject from the date of withdrawal/last contact.

Investigators made an attempt to contact those subjects who did not return for scheduled visits or follow-up.

Information relative to the withdrawal was documented in the eCRF. The investigator documented whether the decision to withdraw a subject from the study was made by the subject's parent(s) or LAR(s), or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- SAE
- Non-serious AE
- Protocol violation (specify)
- Consent withdrawal, not due to an AE*
- Moved from the study area
- Lost to follow-up
- Other (specify)

*In case a subject was withdrawn from the study because the subject's parent(s)/LAR(s) had withdrawn consent, the investigator documented the reason for withdrawal of consent, if specified by the subject, in the eCRF.

Subjects who were withdrawn from the study because of SAEs/AEs had to be clearly distinguished from subjects who were withdrawn for other reasons. Investigators followed subjects who were withdrawn from the study as result of an SAE/AE until resolution of the event.

5.3.4.2.2. Subject withdrawal from investigational vaccine/product

A 'withdrawal' from the investigational vaccine referred to any subject who did not receive the complete treatment, i.e., when no further planned dose was administered from the date of withdrawal. A subject withdrawn from the investigational vaccine could not necessarily be withdrawn from the study as further study procedures or follow-up could be performed (safety or immunogenicity) if planned in the study protocol.

Information relative to premature discontinuation of the investigational vaccine was documented on the Vaccine Administration screen of the eCRF. The investigator documented whether the decision to discontinue further vaccination/treatment was made by the subject's parent(s)/LAR(s), or by the investigator, as well as which of the following possible reasons were responsible for withdrawal:

- SAE
- Non-serious AE
- Other (specify)

5.4. Composition and administration of vaccines

5.4.1. Description of vaccines

The control vaccine (*Fluarix*) and the candidate vaccine (FLU Q-QIV) were developed and manufactured by GSK Biologicals and had a thimerosal-free formulation.

***Fluarix* (D-TIV-YB)**

The TIV *Fluarix* vaccine contained HA from three influenza strains, with a total HA content of 45 µg, recommended for the influenza season 2012-2013 by the WHO, CDC/CBER, and European Medicines Agency (EMEA)/Committee for Medicinal Products for Human Use (CHMP):

- H1N1 strain: A/California/7/2009 (H1N1 pdm09) (15 µg)
- H3N2 strain: A/Victoria/361/2011 (H3N2) (15 µg)
- B strain (Yamagata lineage): B/Hubei-Wujiagang/158/09 (15 µg)

The excipients used in the *Fluarix* formulations complied with the United States and/or European Pharmacopoeia (see Table 7).

Commercial vaccines were assumed to comply with the specifications given in the manufacturer's Summary of Product Characteristics (SPC).

FLU Q-QIV

The FLU Q-QIV vaccine used in the study had a total HA content of 60 µg.

It contained the same influenza A-like and B strains as those described for *Fluarix* above, as well as the most recently WHO, CDC/CBER, and EMEA/CHMP recommended B strain from the lineage not included in the 2012-2013 WHO recommendations, i.e., B/Brisbane/60/2008 like virus (15 µg):

- H1N1 strain: A/California/7/2009 (H1N1 pdm09) (15 µg)
- H3N2 strain: A/Victoria/361/2011 (H3N2) (15 µg)
- B strain (Victoria lineage): B/Brisbane/60/2008 (15 µg)
- B strain (Yamagata lineage): B/Hubei-Wujiagang/158/09 (15 µg)

The excipients used in the FLU Q-QIV formulation complied with the United States and/or European Pharmacopoeia (see Table 7).

The Quality Control Standards and Requirements for the candidate vaccine were described in separate Quality Assurance documents (e.g., release protocols, certificate of analysis) and the required approvals had been obtained.

The tip caps of the prefilled syringes could contain natural rubber latex which could cause allergic reactions in latex sensitive individuals; therefore latex had to be considered a component of the vaccines.

The vaccines were labelled and packed according to applicable regulatory requirements.

Table 7 Study vaccines

Treatment name	Vaccine name	Formulation	Presentation	Volume	Number of doses	Lot numbers
Q-QIV	FLU Q-QIV	Sodium chloride, potassium chloride, sodium phosphate dibasic heptahydrate, potassium phosphate monobasic, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80) and water for injection	Translucent to off-white/greyish opalescent suspensions that could sediment slightly, presented in prefilled syringes	0.5 mL	1 (primed subjects) 2 (unprimed subjects)	DFLHA760A
D-TIV-YB	*Fluarix*	Sodium chloride, disodium phosphate dodecahydrate, potassium dihydrogen phosphate, potassium chloride, magnesium chloride hexahydrate, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), octoxynol 10 (Triton X-100), and water for injection.	Translucent to off-white/greyish opalescent suspensions that could sediment slightly, presented in prefilled syringes	0.5 mL	1 (primed subjects) 2 (unprimed subjects)	AFLUA726A

5.4.2. Dosage and administration of study vaccines

Primed subjects received a single 0.5 mL dose administered IM on Day 0. Unprimed subjects received two 0.5 mL doses administered IM on Day 0 and Day 28.

The buttock was not used for administration of vaccines because of the potential risk of injury to the sciatic nerve and the risk of decreased immunogenicity due to inadvertent subcutaneous injection or injection into deep fat tissue.

The needle for any IM injection had to be long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underlying nerves and blood vessels or bone. For injection into either the deltoid muscle or anterolateral region of the thigh, a 25 Mm (1 inch), 22-25 gauge needle was typically used. Although it was recommended to follow this guideline, an individual decision on needle size and site of injection had to be made for each person on the basis of age and muscle size. Vaccinators had to be familiar with the anatomy of the area into which they were injecting the vaccine.

The vaccine recipients were observed closely for at least 30 minutes following the administration of vaccine, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.

The vaccines were administered as indicated in Table 8 (subjects < 12 months of age) and Table 9 (subjects ≥ 12 months of age).

Table 8 Dosage and administration for subjects below 12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route [1]	Site [2]	Side
Visit Day 0	0.5 mL	Q-QIV PRIM	Q-QIV	IM	Anterolateral thigh	Left
		Q-QIV UNPRIM				
Visit Day 28	0.5 mL	Q-QIV UNPRIM				
Visit Day 0	0.5 mL	D-TIV-YB PRIM	D-TIV-YB	IM	Anterolateral thigh	Left
		D-TIV-YB UNPRIM				
Visit Day 28	0.5 mL	D-TIV-YB UNPRIM				

[1]Intramuscular (IM)
[2]Thigh injection was the recommended route for subjects < 12 months of age, however the other route (deltoid) could be considered based on the individual anatomy.

Table 9 Dosage and administration for subjects greater than or equal to 12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route [1]	Site [2]	Side
Visit Day 0	0.5 mL	Q-QIV PRIM	Q-QIV	IM	Deltoid	Non-dominant
		Q-QIV UNPRIM				
Visit Day 28	0.5 mL	Q-QIV UNPRIM				
Visit Day 0	0.5 mL	D-TIV-YB PRIM	D-TIV-YB	IM	Deltoid	Non-dominant
		D-TIV-YB UNPRIM				
Visit Day 28	0.5 mL	D-TIV-YB UNPRIM				

[1]Intramuscular (IM)
[2]Deltoid injection was the recommended route for subjects ≥ 12 months of age, however the other route (thigh) could be considered based on the individual anatomy.

5.4.3. Contraindications to subsequent vaccination

The following events constituted absolute contraindications to further administration of the FLU Q-QIV vaccine. If any of these events occurred during the study, the subject should not have received additional doses of vaccine but could continue other study procedures at the discretion of the investigator.

- Anaphylaxis following the administration of vaccine(s).

The following events constituted contraindications to administration of the study vaccines at that point in time; if any of these events occurred at the time scheduled for vaccination, the subject could be vaccinated at a later date, within the time window specified in the protocol (see Section 5.2.2), or the subject could be withdrawn at the discretion of the investigator.

- Acute disease and/or fever at the time of vaccination.
  - Fever was defined as temperature ≥ 38.0°C/100.4°F by any method.
  - Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever could be administered all vaccines.

5.4.4. Warnings and precautions

Refer to the approved product label/package insert for *Fluarix*.

5.4.5. Treatment allocation and randomisation

5.4.5.1. Randomisation of supplies

The randomisation of supplies within blocks was performed at GSK Biologicals, using MATerial EXcellence (MATEX), a program developed for use in Statistical Analysis System (SAS®) (Cary, NC, USA) by GSK Biologicals. Entire blocks were shipped to the study centres/warehouse(s).

To allow GSK Biologicals to take advantage of greater rates of recruitment than anticipated at individual centres in this multi-centre study and to thus reduce the overall study recruitment period, an over-randomisation of supplies was prepared.

5.4.5.2. Treatment allocation to the subject

The treatment numbers were allocated by dose. Each dose had a single unique treatment number throughout the study.

5.4.5.2.1. Study group and treatment number allocation

The target was to enrol approximately 600 eligible subjects who were randomly assigned to two study groups in a 1:1 ratio (approximately 300 subjects in each group).

The enrolment was performed to ensure equal distribution of the population across the two study groups, i.e., the two study groups had similar demographic characteristics (priming status, age and centre). To achieve this, allocation of the subject to a study group at the investigator site was performed using a randomisation system on internet (SBIR). Within each priming status (primed or unprimed), the randomisation algorithm used a minimisation procedure accounting for age (6 to 17 months old and 18 to 35 months old) and centre. Minimisation factors had equal weight in the minimisation algorithm.

After obtaining the signed and dated informed consent form (ICF) from the subject's parent(s)/LAR(s) and having checked the eligibility of the subject, the study staff in charge of the vaccine administration accessed SBIR. Upon providing the priming status, age and the subject identification number, the randomisation system determined the study group and provided the treatment number to be used for each dose.

The number of each administered treatment had to be recorded in the eCRF on the Vaccine Administration screen.

When SBIR was not available, a reference to the SBIR user guide or the Study Procedures Manual (SPM) was made for specific instructions.

Note that as soon as the total target number of 600 subjects had been reached, the enrolment was to be frozen.

5.4.5.2.2. Treatment number allocation for subsequent doses

For each dose subsequent to the first dose, the study staff in charge of the vaccine administration accessed SBIR, provided the subject identification number, and the system provided a treatment number consistent with the allocated study group.

The number of each administered treatment had to be recorded in the eCRF on the Vaccine Administration screen.

5.5. Blinding

Data were collected in a double-blind manner.

The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

GSK Biologicals' policy (which incorporates International Conference on Harmonisation [ICH] E2A guidance, EU Clinical Trial Directive and US Federal Regulations) was to unblind the report of any SAE which was unexpected and attributable/suspected to be attributable to the investigational vaccine/product, prior to regulatory reporting. The GSK Biologicals' Central Safety Physician was responsible for unblinding the treatment assignment in accordance with the specified timeframes for expedited reporting of SAEs.

Unblinding of a subject's individual treatment code had to occur only in the case of a medical emergency, or in the event of a serious medical condition, when knowledge of the study treatment was essential for the clinical management or welfare of the subject, as judged by the investigator.

The emergency unblinding process consisted of the automated system SBIR that allowed the investigator to have unrestricted, immediate and direct access to the subject's individual study treatment.

The investigator had the option of contacting a GSK Biologicals' On-call Central Safety Physician (or backup) if he/she needed medical advice or needed the support of GSK to perform the unblinding (i.e., he/she could not access SBIR).

Any emergency unblinding had to be fully documented by using the Emergency Unblinding Documentation Form, which had to be appropriately completed by the investigator and sent within 24 hours to GSK Biologicals.

5.6. Prior and concomitant medication/vaccinations

At each study visit/contact, the investigator was to question the subject's parent(s)/LAR(s) about any medication/product taken and vaccination received by the subject.

The following concomitant medications/products/vaccines were to be recorded in the eCRF if administered during the indicated recording period:

- All concomitant medications/products, except vitamins and dietary supplements administered 30 days following each dose of study vaccine.

- Any concomitant vaccination administered in the period starting 30 days before the first dose of study vaccine and ending at the last study contact.
- Prophylactic medication (i.e., medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination).

  E.g., an antipyretic was considered to be prophylactic when it was given in the absence of fever and any other symptom, to prevent fever from occurring [fever was defined as temperature ≥ 38.0°C/100.4°F by any method].
- Any antipyretic administered in the period starting 6 hours before vaccination and ending 12 hours after vaccination.
- Any concomitant medications/products/vaccines listed in Section 5.3.3.
- Any concomitant medication/product/vaccine relevant to an SAE* or administered at any time during the study period for the treatment of an SAE*.

  * SAEs that were required to be reported per protocol.

5.7. Laboratory assays and time points

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

5.8. Assessment of immunogenicity variables

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

5.9. Assessment of safety variables

The investigator or site staff was/were responsible for the detection, documentation and reporting of events meeting the criteria and definition of an AE or SAE as provided in the protocol.

Each subject's parent(s)/LAR(s) were instructed to contact the investigator immediately should the subject manifest any signs or symptoms they perceived as serious.

5.9.1. Adverse events

An AE was any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An AE could therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also included failure to produce expected benefits (i.e., lack of efficacy), abuse or misuse.

Examples of an AE included:

- Significant or unexpected worsening or exacerbation of the condition/indication under study.
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after investigational vaccine administration even though they could have been present prior to the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either investigational vaccine or a concurrent medication (overdose per se did not have to be reported as an AE/SAE).
- Signs, symptoms temporally associated with vaccine administration.
- Significant failure of expected pharmacological or biological action.
- Pre- or post-treatment events that occurred as a result of protocol-mandated procedures (i.e., invasive procedures, modification of subject's previous therapeutic regimen).

AEs recorded as endpoints (solicited AEs) are described in Section 5.9.1.1. All other AEs were recorded as unsolicited AEs.

Examples of an AE did NOT include:

- Medical or surgical procedures (e.g., endoscopy, appendectomy); the condition that led to the procedure was an AE/SAE.
- Situations where an untoward medical occurrence did not occur (e.g., social and/or convenience admission to a hospital, admission for routine examination).
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that did not worsen.
- Pre-existing conditions or signs and/or symptoms present in a subject prior to the first study vaccination. These events were recorded in the medical history section of the eCRF.

5.9.1.1. Solicited adverse events

Solicited AEs occurring during the 7-day follow-up period after vaccination were recorded. Solicited local (injection-site) and general AEs recorded are summarised in Table 10 and Table 11, respectively.

The following local (injection-site) AEs were solicited:

Table 10 Solicited local adverse events

Pain at injection site
Redness at injection site
Swelling at injection site

The following general AEs were solicited:

Table 11 Solicited general adverse events

Drowsiness
Fever
Irritability/Fussiness
Loss of appetite

Note: Temperature was to be recorded in the evening. If additional temperature measurements were performed at other times of day, the highest temperature was to be recorded in the eCRF.

5.9.1.2. Assessment of intensity

The intensity of the following solicited AEs was assessed as described in Table 12.

Table 12 Intensity scales for solicited symptoms in infants/toddlers and children less than 6 years of age

Infant/Toddler (15–24 months)/Child (< 6 years)		
Adverse Event	**Intensity grade**	**Parameter**
Pain at injection site	0	None
	1	Mild: Minor reaction to touch
	2	Moderate: Cried/protested on touch
	3	Severe: Cried when limb was moved/spontaneously painful
Redness at injection site		Recorded greatest surface diameter in mm
Swelling at injection site		Recorded greatest surface diameter in mm
Fever*		Recorded temperature in °C/°F
Irritability/Fussiness	0	Behaviour as usual
	1	Mild: Cried more than usual/no effect on normal activity
	2	Moderate: Cried more than usual/interfered with normal activity
	3	Severe: Crying that could not be comforted/prevented normal activity
Drowsiness	0	Behaviour as usual
	1	Mild: Drowsiness easily tolerated
	2	Moderate: Drowsiness that interfered with normal activity
	3	Severe: Drowsiness that prevented normal activity
Loss of appetite	0	Appetite as usual
	1	Mild: Ate less than usual/no effect on normal activity
	2	Moderate: Ate less than usual/interfered with normal activity
	3	Severe: Did not eat at all

*Fever was defined as temperature ≥ 38.0°C / 100.4°F by any method

The maximum intensity of local injection site redness/swelling was scored at GSK Biologicals as follows:

0 : ≤ 20 mm
1 : > 20 - ≤ 50 mm
2 : > 50 - ≤ 100 mm
3 : > 100 mm

The grade of fever was scored as follows:

1	:	≥ 38.0°C (100.4°F) - ≤ 38.5°C (101.3°F)
2	:	> 38.5°C (101.3°F) - ≤ 39.0°C (102.2°F)
3	:	> 39.0°C (102.2°F) - ≤ 40.0°C (104°F)
4	:	> 40.0°C (104°F)

The investigator assessed the maximum intensity that occurred over the duration of the event for all unsolicited AEs (including SAEs) recorded during the study. The assessment was based on the investigator's clinical judgement.

The intensity was to be assigned to one of the following categories:

1 (mild)	=	An AE which was easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE which was sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE which prevented normal, everyday activities. (In a young child, such an AE would, for example, prevent attendance at kindergarten/a day-care centre and would cause the parent(s)/LAR(s) to seek medical advice.)

An AE that was assessed as Grade 3 (severe) did not have to be confused with an SAE. Grade 3 was a category used for rating the intensity of an event; and both AEs and SAEs could be assessed as Grade 3. An event was defined as 'serious' when it met one of the pre-defined outcomes as described in Section 5.9.2.

5.9.1.3. Assessment of causality

The definitions for 'NO' and 'YES' had been written in such a way that all events that had been attributed a 'NO' could be pooled with events which in the primary vaccination study were determined to be 'not related' or 'unlikely to be related' to vaccination. Those events that were attributed a 'YES' could be pooled with those events that in the past were determined to have a 'suspected' or 'probable' relationship to vaccination in the primary vaccination study.

The investigator was obligated to assess the relationship between investigational vaccine and the occurrence of each AE/SAE. The investigator used clinical judgement to determine the relationship. Alternative plausible causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational vaccine were considered and investigated. The investigator also consulted the Investigator Brochure (IB) and/or PI for marketed products to determine his/her assessment.

There could be situations when an SAE had occurred and the investigator had minimal information to include in the initial report to GSK Biologicals. However, it was very important that the investigator always made an assessment of causality for every event prior to submission of the SAE report to GSK Biologicals. The investigator could change

his/her opinion of causality in light of follow-up information and update the SAE information accordingly. The causality assessment was one of the criteria used when determining regulatory reporting requirements.

In case of concomitant administration of multiple vaccines, it could not be possible to determine the causal relationship of general AEs to the individual vaccines administered. Therefore, the investigator had to assess whether the AE could be causally related to vaccination rather than to the individual vaccines.

All solicited local (injection site) AEs were considered causally related to vaccination. Causality of all other AEs had to be assessed by the investigator using the following question:

Was there a reasonable possibility that the AE could have been caused by the investigational vaccine/product?

YES : There was a reasonable possibility that the vaccine(s) contributed to the AE.

NO : There was no reasonable possibility that the AE was causally related to the administration of the study vaccine(s). There were other, more likely causes and administration of the study vaccine(s) was not suspected to have contributed to the AE.

If an event met the criteria to be determined as 'serious' (see Section 5.9.2), additional examinations/tests were performed by the investigator in order to determine ALL possible contributing factors for each SAE.

Possible contributing factors included:

- Medical history
- Other medication
- Protocol required procedure
- Other procedure not required by the protocol
- Lack of efficacy of the vaccine, if applicable
- Erroneous administration
- Other cause (specified)

5.9.1.4. Assessments of outcomes

The investigator assessed the outcome of all unsolicited AEs (including SAEs) recorded during the study as:

- Recovered/resolved
- Recovering/resolving
- Not recovered/not resolved
- Recovered with sequelae/resolved with sequelae
- Fatal (SAEs only)

5.9.1.5. Treatment of adverse events

Treatment of any AE was at the sole discretion of the investigator and according to current good medical practice. Any medication administered for the treatment of an AE had to be recorded in the subject's eCRF (refer to Section 5.6).

5.9.1.6. Medically attended visits

For each solicited and unsolicited symptom the subject experienced, the subject's parent(s)/LAR(s) were asked if the subject received medical attention defined as hospitalisation, or an otherwise unscheduled visit to or from medical personnel for any reason, including emergency room visits. This information was recorded in the eCRF.

5.9.1.7. Potential immune-mediated diseases

PIMDs are a subset of AEs that included autoimmune diseases and other inflammatory and/or neurologic disorders of interest which could or could not have an autoimmune aetiology. AEs that needed to be recorded and reported as pIMDs included those listed in Table 13.

However, the investigator exercised his/her medical and scientific judgement in deciding whether other diseases had an autoimmune origin (i.e., pathophysiology involving systemic or organ-specific pathogenic autoantibodies) and also had to be recorded as a pIMD.

Table 13 List of potential immune-mediated diseases

Neuroinflammatory disorders	Musculoskeletal disorders	Skin disorders
• Cranial nerve disorders, including paralyses/paresis (e.g., Bell's palsy) • Optic neuritis • Multiple sclerosis • Transverse myelitis • Guillain-Barré syndrome, including Miller Fisher syndrome and other variants • Acute disseminated encephalomyelitis, including site specific variants: e.g., non-infectious encephalitis, encephalomyelitis, myelitis, myeloradiculomyelitis • Myasthenia gravis, including Lambert-Eaton myasthenic syndrome • Immune-mediated peripheral neuropathies and plexopathies, (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy). • Narcolepsy	• Systemic lupus erythematosus • Scleroderma, including diffuse systemic form and CREST syndrome • Systemic sclerosis • Dermatomyositis • Polymyositis • Antisynthetase syndrome • Rheumatoid arthritis, • Juvenile chronic arthritis, (including Still's disease) • Polymyalgia rheumatic • Spondyloarthritis, including ankylosing spondylitis, reactive arthritis (Reiter's Syndrome) and undifferentiated spondyloarthritis • Psoriatic arthropathy • Relapsing polychondritis • Mixed connective tissue disorder	• Psoriasis • Vitiligo • Erythema nodosum • Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis) • Cutaneous lupus erythematosus • Alopecia areata • Lichen planus • Sweet's syndrome • Morphoea

Liver disorders	Gastrointestinal disorders	Metabolic diseases
• Autoimmune hepatitis • Primary biliary cirrhosis • Primary sclerosing cholangitis • Autoimmune cholangitis	• Crohn's disease • Ulcerative colitis • Ulcerative proctitis • Celiac disease	• Autoimmune thyroiditis (including Hashimoto thyroiditis) • Grave's or Basedow's disease • Diabetes mellitus type I • Addison's disease

Vasculitides	Others
• Large vessels vasculitis including: giant cell arteritis such as Takayasu's arteritis and temporal arteritis. • Medium sized and/or small vessels vasculitis including: polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg–Strauss syndrome (allergic granulomatous angiitis), Buerger's disease (thromboangiitis obliterans), necrotizing vasculitis and anti-neutrophil cytoplasmic antibody (ANCA) positive vasculitis (type unspecified), Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis.	• Autoimmune hemolytic anemia • Autoimmune thrombocytopenia • Antiphospholipid syndrome • Pernicious anemia • Autoimmune glomerulonephritis (including IgA nephropathy, glomerulonephritis rapidly progressive, membranous glomerulonephritis, membranoproliferative glomerulonephritis, and mesangioproliferative glomerulonephritis) • Uveitis • Autoimmune myocarditis/cardiomyopathy • Sarcoidosis • Stevens-johnson syndrome • Sjögren's syndrome • Idiopathic pulmonary fibrosis • Goodpasture syndrome • Raynaud's phenomenon

Note: This list was based on the Medical Dictionary for Regulatory Activities (MedDRA), Version 15. The data cleaning and analysis for pIMDs had to be adjusted accordingly if the MedDRA dictionary for pIMDs was updated.

When there was enough evidence to make any of the diagnoses listed in Table 13, the AE had to be reported as a pIMD. Symptoms, signs or conditions which could (or could not) represent the diagnoses, had to be recorded and reported as AEs but not as pIMDs until the final or definitive diagnosis had been determined, and alternative diagnoses had been eliminated or shown to be less likely.

In order to facilitate the documentation of pIMDs in the eCRF, a pIMD standard questionnaire and a list of preferred terms (PTs) and PT codes corresponding to the diagnoses was available to investigators at study start.

5.9.2. Serious adverse events

An SAE was any untoward medical occurrence that:

a. Resulted in death.

b. Was life-threatening.

   Note: The term 'life-threatening' in the definition of 'serious' referred to an event in which the subject was at risk of death at the time of the event. It did not refer to an event, which hypothetically could have caused death, had it been more severe.

c. Required hospitalisation or prolongation of existing hospitalisation.

   Note: In general, hospitalisation signified that the subject had been admitted at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or in an out-patient setting. Complications that occurred during hospitalisation were also considered AEs. If a complication prolonged hospitalisation or fulfilled any other serious criteria, the event was also considered serious. When in doubt as to whether 'hospitalisation' occurred or was necessary, the AE had to be considered serious.

   Hospitalisation for elective treatment of a pre-existing condition (known or diagnosed prior to informed consent signature) that did not worsen from baseline was NOT considered an AE.

d. Resulted in disability/incapacity.

   Note: The term disability meant a substantial disruption of a person's ability to conduct normal life functions. This definition was not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhoea, influenza like illness, and accidental trauma (e.g., sprained ankle) which could interfere or prevent everyday life functions but did not constitute a substantial disruption.

Medical or scientific judgement were to be exercised in deciding whether reporting was appropriate in other situations, such as important medical events that could not be immediately life-threatening or resulted in death or hospitalisation but could jeopardise the subject or could require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These also were to be considered serious. Examples of such events were invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalisation.

5.9.2.1. Time period for detecting and recording adverse events and serious adverse events

All AEs starting within 28 days following administration of each dose of study vaccine/comparator were recorded into the appropriate section of the eCRF, irrespective of intensity or whether or not they were considered vaccination-related.

The time period for collecting and recording SAEs and pIMDs began at the first receipt of study vaccine/comparator and ended 180 days following administration of the last dose of study vaccine/comparator for each subject.

All AEs/SAEs leading to withdrawal from the study were collected and recorded from the time of the first receipt of study vaccine/comparator.

SAEs that were related to the investigational vaccine were collected and recorded from the time of the first receipt of study vaccine/comparator until the subject was discharged from the study.

In addition to the above-mentioned reporting requirements and in order to fulfil international reporting obligations, SAEs that were related to study participation (i.e., protocol-mandated procedures, invasive tests, a change from existing therapy) or were related to a concurrent GSK medication/vaccine were collected and recorded from the time the subject consented to participate in the study until she/he was discharged from the study.

An overview of the protocol-required reporting periods for AEs and SAEs is given in Table 14.

A post-study AE/SAE was defined as any event that occurred outside of the AE/SAE reporting period defined in Table 14. The investigator was not obligated to actively seek AEs or SAEs in former study participants. However, if the investigator learned of any SAE at any time after a subject had been discharged from the study, and he/she considered the event reasonably related to the investigational vaccine/product, the investigator promptly had to notify the Study Contact for Reporting SAEs.

Table 14 Reporting periods for adverse events and serious adverse events

Event	Pre-Vacc*	Vacc 1	7 days post-Vacc 1	28 days post-Vacc 1	Vacc 2**	6 days post-Vacc 2**	28 days post-Vacc 2**	6 months post-Vacc 1
Time point		Day 0	Day 6	Day 27	Day 28	Day 34	Day 56	Day 180
Solicited local and general AEs								
Unsolicited AEs								
AEs/SAEs leading to withdrawal from the study								
SAEs related to the investigational vaccine/product								
SAEs related to study participation or concurrent GSK medication/vaccine								
SAEs, MAEs, pIMDs								
Recording of intercurrent medical conditions								

Vacc = vaccination; Pre-Vacc = pre-vaccination; (S)AE = (Serious) Adverse Event; pIMD = potential Immune-Mediate Disease; MAE = Medically Attended Adverse Event
*Informed consent obtained
**Only for unprimed subject

5.9.2.2. Evaluation of adverse events and serious adverse events

As a consistent method of collecting AEs, the subject's parent(s)/LAR(s) had to be asked a non-leading question such as:

'*Did your child act differently or feel different in any way since receiving the vaccine or since the last visit?*'

When an AE/SAE occurred, it was the responsibility of the investigator to review all documentation (e.g., hospital progress notes, laboratory and diagnostics reports) relative to the event. The investigator then recorded all relevant information regarding an AE/SAE in the eCRF. The investigator was not allowed to send photocopies of the subject's medical records to GSK Biologicals instead of appropriately completing the eCRF. However, there could be instances when copies of medical records for certain cases were requested by GSK Biologicals. In this instance, all subject identifiers were blinded on the copies of the medical records prior to submission to GSK Biologicals.

The investigator attempted to establish a diagnosis pertaining to the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis had to be documented as the AE/SAE and not the individual signs/symptoms.

5.9.2.3. Reporting of serious adverse events and other events

SAEs and pIMDs were reported promptly to GSK within the timeframes described in Table 15, once the investigator determined that the event met the protocol definition of an SAE.

Table 15 Timeframes for submitting serious adverse event and other events reports to GlaxoSmithKline (GSK) Biologicals

Type of Event	Initial Reports		Follow-up of Relevant Information on a Previous Report	
	Timeframe	Documents	Timeframe	Documents
SAEs	24 hours*	electronic SAE report	24 hours*	electronic SAE report
pIMDs	24 hours**	electronic SAE report	24 hours*	electronic SAE report

* Timeframe allowed after receipt or awareness of the information.
**Timeframe allowed after the diagnosis was established and known to the investigator.

Once an investigator became aware that an SAE had occurred in a study subject, the investigator (or designate) had to complete the information in the electronic SAE report WITHIN 24 HOURS. The SAE report was always completed as thoroughly as possible with all available details of the event. Even if the investigator did not have all information regarding an SAE, the report still had to be completed within 24 hours. Once additional relevant information was received, the report had to be updated WITHIN 24 HOURS.

The investigator always provided an assessment of causality at the time of the initial report.

If the electronic SAE reporting system did not work, the investigator (or designate) had to complete, then date and sign a paper SAE report and fax it to the GSK Biologicals Clinical Safety and Pharmacovigilance department within 24 hours.

This back-up system only had to be used if the electronic SAE reporting system was not working and NOT if the system was slow. As soon as the electronic SAE reporting system was working again, the investigator (or designate) had to complete the electronic SAE report within 24 hours. The final valid information for regulatory reporting was the information reported through the electronic SAE reporting system.

Once onset of a new pIMD or exacerbation of a pre-existing pIMD was diagnosed (serious or non-serious) in a study subject, the investigator (or designate) had to complete the information in the electronic SAE report WITHIN 24 HOURS after he/she became aware of the diagnosis. A field on the SAE report allowed to specify that the event was a pIMD and whether it was serious or non serious. The SAE report was always completed as thoroughly as possible with all available details of the event, in accordance with the pIMD standard questionnaire provided. Even if the investigator did not have all information regarding a pIMD, the report still had to be completed within 24 hours. Once additional relevant information was received, the report had to be updated WITHIN 24 HOURS.

The investigator always provided an assessment of causality at the time of the initial report.

When additional SAE or pIMD information was received after freezing of the subject's eCRF, new or updated information had to be recorded on a paper report, with all changes signed and dated by the investigator. The updated report had to be faxed to the GSK Biologicals Clinical Safety and Pharmacovigilance department or to the Study Contact for Reporting SAEs (refer to the Sponsor Information Sheet) within the designated reporting time frames specified in Table 15.

The investigator promptly reported all SAEs to GSK. GSK Biologicals had a legal responsibility to promptly notify, as appropriate, both the local regulatory authority and other regulatory agencies about the safety of a product under clinical investigation. Prompt notification of SAEs by the investigator to the Study Contact for Reporting SAEs was essential so that legal obligations and ethical responsibilities towards the safety of other subjects were met.

Investigator safety reports were prepared according to the current GSK policy and were forwarded to investigators as necessary. An investigator safety report was prepared for an SAE(s) that was both attributable to the investigational vaccine/product and unexpected. The purpose of the report was to fulfil specific regulatory and GCP requirements, regarding the product under investigation.

5.9.2.4. Follow-up of adverse events and serious adverse events

After the initial AE/SAE report, the investigator was required to proactively follow each subject and provide additional relevant information on the subject's condition to GSK Biologicals (within 24 hours for SAEs; refer to Table 15).

All SAEs and pIMDs (serious or non-serious) documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were reviewed at subsequent visits/contacts until the end of the study.

With the exception of MAEs and pIMDs, all AEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were reviewed at subsequent visits/contacts until 30 days after the last vaccination.

The investigator followed subjects:

- with SAEs, pIMDs (serious or non-serious), or subjects withdrawn from the study as a result of an AE, until the event had resolved, subsided, stabilised, disappeared, or until the event was otherwise explained, or the subject was lost to follow-up.
- with MAEs or pIMDs not recovered/resolved at previous contact or visit, until the end of the study or the subjects were lost to follow-up.
- with other non-serious AEs, until Day 28 (primed subjects) or Day 56 (unprimed subjects) or they were lost to follow-up.

If the investigator received additional relevant information on a previously reported SAE, he/she provided this information to GSK Biologicals using a paper SAE report.

GSK Biologicals could request that the investigator performed or arranged the conduct of additional clinical examinations/tests and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE or SAE. The investigator was obliged to assist. If a subject died during participation in the study or during a recognised follow-up period, GSK Biologicals was provided with any available post-mortem findings, including histopathology.

5.9.3. Clinical laboratory evaluations

In absence of diagnosis, abnormal laboratory findings (e.g., clinical chemistry, haematology, urinalysis) or other abnormal assessments (e.g., physical examination findings) that were judged by the investigator to be clinically significant were recorded as AE or SAE if they met the definition of an AE or SAE (refer to Sections 5.9.1 and 5.9.2). Clinically significant abnormal laboratory findings or other abnormal assessments that were present at baseline and significantly worsened following the start of the study were also reported as AEs or SAEs. However, clinically significant abnormal laboratory findings or other abnormal assessments that were associated with the disease being studied, unless judged by the investigator as more severe than expected for the subject's condition, or that were present or detected at the start of the study and did not worsen, were not reported as AEs or SAEs.

The investigator exercised his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment was clinically significant.

5.10. Statistical methods

The statistical methods below are specific to the analyses presented in this Annex Report. All other statistical methods were described in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report.

Statistical methods were performed as per protocol and Statistical Analysis Plan (SAP).

The statistical analyses were performed using the SAS version 9.2 on Windows and StatXact-7.0 procedure on SAS.

5.10.1. Secondary Outcome/Efficacy Variables

- SAEs, MAEs, and pIMDs
  - Occurrence of SAEs, MAEs, and pIMDs (summarised by incidence rate and relationship to vaccination) during the entire study period.

5.10.2. Determination of sample size

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

5.10.3. Study cohorts /data sets analysed

5.10.3.1. Total Vaccinated cohort

The Total Vaccinated cohort (TVC) included all vaccinated subjects for whom data were available. For the total analysis of safety, this included all vaccinated subjects for whom safety data were available.

The TVC analysis was performed per treatment actually administered.

5.10.3.2. According-to-protocol cohort for analysis of safety

The ATP cohort for analysis of safety included all vaccinated subjects

- Who received at least one dose of study vaccine/comparator according to their random assignment.
- With sufficient data to perform an analysis of safety.
- For whom administration site of study vaccine/comparator was known.
- Who had not received a vaccine not specified or forbidden in the protocol.

5.10.4. Derived and transformed data

For the analysis of MAEs and SAEs, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.

5.10.5. Analysis of demographics

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

5.10.6. Analysis of immunogenicity

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

5.10.7. Analysis of safety

The primary analysis was performed on the TVC. Should the percentage of subjects excluded from the TVC be greater than 5%, a second analysis was to be performed on the ATP cohort for safety to complement the analysis of the TVC.

5.10.7.1. Within-groups assessment

The safety analyses mentioned below are specific to the objective presented in this Annex Report. All other safety analyses of the study were described in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report.

- SAEs, MAEs, and pIMDs were collected and summarised until Day 56 and through the entire follow-up period. In addition, SAEs and withdrawal due to AEs were described in detail.
- The percentage of subjects reporting AEs resulting in a medically attended visit was also tabulated.

5.10.8. Sequence of analyses

Two final analyses were performed.

The first analysis included safety and immunogenicity data as clean as possible up to Day 56 and is presented in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report.

The second analysis was performed following the 6-month safety follow-up completion and is presented in this Annex Report. This analysis was performed on clean data.

Until the last analysis was released, access to individual treatment codes was restricted to the statistician in charge of the analyses and authorised staff.

5.10.9. Interim analysis

There was no interim analysis. All analyses were conducted on final data and therefore no statistical adjustment for multiple analyses was required.

5.11. Data quality assurance at study level

To ensure that the study procedures conformed across all investigator sites, the protocol, eCRF and safety reporting were reviewed with the investigator(s) and his/her/their personnel responsible for the conduct of the study by the Company representative(s) prior to study start. A multi-investigator meeting was held prior to the study start.

Adherence to the protocol requirements and verification of data generation accuracy were achieved through monitoring visits to each investigator site. Computer checks and blinded review of subject tabulations were performed to ensure consistency of eCRF completion. All procedures were performed according to methodologies detailed in GSK Biologicals Standard Operating Procedures (SOPs).

During the course of the study, issues with regard to the conduct of the study were identified, either via site monitoring activities or were brought to GSK Biologicals' attention by other oversight mechanisms. These issues were investigated and corrective and/or preventive actions where possible were taken as described in Section 6.2.3.2.

Contract Research Organisations (CROs), Emtex, Keyrus Biopharma and Business & Decision, were employed to perform medical writing, data management and laboratory management, respectively, according to an agreed contract. The CRO responsibilities were conducted according to GSK SOPs.

Two issues impacting the electronic data capture system (e-N@ble Web system) used in this study were detected between April and May 2013. The technical root cause of these incidents has been identified. Corrective actions are in progress since August 2013 and are planned to be completed by December 2013. There is no impact on subject safety.

1. The signatory displayed on some signature screens in the e-N@ble Web system may be incorrect until the issue will be fixed for this study. After successful correction of the signature display, there will be no impact on data integrity. The issue is at the level of the display: only investigators were authorised to sign off data, and only investigators have signed off data.

2. In the audit trail, while the author, date and time of original entry and data changes are correct, the reason for changes has been overwritten. All reasons for data change collected before the fix of the issue are considered as not reliable and hence the integrity of the audit trail data is impacted; the reason for change are not part of the analysed data.

Independent Audit statement:

- This study was subject to audit by GlaxoSmithKline's department of Worldwide Regulatory Compliance-GCP (WRC-GCP) at two sites (one site in Honduras and one site in Canada).

5.12. Changes in the conduct of the study or planned analyses

5.12.1. Protocol amendments

The original protocol for this study was dated 30 July 2012. There were no protocol amendments.

5.12.2. Other changes

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

6. STUDY POPULATION RESULTS

6.1. Study dates

The first volunteer was enrolled in the study on 01-November-2011 and the last study visit (Day 180) was on 19-June-2013. The data lock point (date of database freeze) occurred on 17-September-2013 for the Day 180 analysis.

6.2. Subject eligibility and attrition from the study

The Total enrolled cohort consisted of 607 subjects, including six subjects who were not vaccinated.

A total of 299 subjects in the Q-QIV group and 302 subjects in the D-TIV-YB group received the study vaccines as planned.

6.2.1. Number of subjects

The number of subjects enrolled in the study by centre is presented in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report.

6.2.2. Study completion and withdrawal from study

The number of subjects vaccinated, completed and withdrawn with the reasons for withdrawal and the number of subjects at each visit and list of withdrawn subjects are presented in Table 16 and Table 17, respectively.

6.2.3. Protocol deviations at subject level

6.2.3.1. Protocol deviations leading to elimination from ATP analyses

The deviations from specifications for intervals between study visits for primed and unprimed subjects are presented in Table 18 and Table 19, respectively. However, there were no subject eliminations for the Day 180 safety contact.

6.2.3.2. Protocol deviations not leading to elimination from ATP analyses

There were seven ICH/GCP-related protocol deviations identified at the site in Honduras during the Day 56 analysis. ICFs were either not signed properly or some of the ICF sections were not completed by the LAR. Appropriate corrective actions have been taken to assure confidence in the integrity of the data and the protection of subject's rights, safety and well-being. Therefore these deviations are not leading to elimination from ATP analyses.

6.3. Demographic characteristics

6.3.1. Total Vaccinated cohort

The demographic characteristics (age, height, weight, BMI, gender, and race) overall, by age strata and by priming status are presented in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report. Vital signs characteristics at pre-vaccination, the number of subjects with documented age at Dose 1 by gender (overall, by age strata and by priming status) and the history of influenza vaccination in the previous three seasons are also presented in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report.

6.3.2. According-to-protocol cohort for immunogenicity

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

6.3.3. According-to-protocol cohort for safety

Since the percentage of subjects excluded from the TVC was less than 5%, no secondary analysis was performed on the ATP cohort for safety for the Day 56 analysis.

For the Day 180 safety follow-up, there were no elimination codes allotted.

7. IMMUNOGENICITY RESULTS

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

8. SAFETY RESULTS

8.1. Data sets analysed

The analysis of safety was performed on the TVC (primary analysis).

Information regarding the number and percentage of subjects who received study vaccine per number of doses received and compliance in returning symptom sheets are detailed in the FLU-Q-QIV-013 (Day 56) Amendment 1 study report.

8.2. Total Vaccinated cohort analysis

8.2.1. Overall incidence of adverse events

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

8.2.2. Solicited local adverse events

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

8.2.3. Solicited general adverse events

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

8.2.4. Unsolicited adverse events

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

8.3. According-to-protocol cohort analysis

The primary analysis of safety was performed on the TVC. Since the percentage of enrolled subjects excluded from the TVC for analysis of safety was less than 5%, no secondary analysis on the ATP cohort for safety was performed for the Day 56 analysis.

For the Day 180 safety follow-up, there were no elimination codes allotted.

8.4. Serious adverse events

The SAE Summary Table is presented in Section 13.1 and the SAE Council for International Organisations of Medical Sciences (CIOMS) reports are presented in Section 13.3.

SAE results are detailed in Table 21 to Table 23.

8.4.1. Fatal events

No subject died during this study up to Day 180.

8.4.2. Non-fatal events

During the entire study period (from Day 0 up to the Day 180 phone contact), a total of 25 non-fatal SAEs were reported for 17 subjects. SAEs were reported for nine (3.0%) and eight (2.6%) subjects in the Q-QIV group and D-TIV-YB group, respectively. All SAEs resolved by the end of the study (Day 180 phone contact).

One of the SAEs reported in this Annex Report, febrile convulsion, was initially reported as an AE in the main study report (Day 56) and upgraded to an SAE by the investigator at GSK's request because febrile convulsion is considered a potential risk under close monitoring. Febrile convulsion was reported in a 18 months old unprimed male subject in the Q-QIV group six hours after dose 1. The case was a simple partial convulsion with eyeball rolling and mild stiffness of the upper extremities that lasted about eight seconds. The case was considered related to the study vaccine by the investigator, with no concomitant infections reported. The subject was attended at the emergency room but not hospitalized, and recovered with no sequela. Dose 2 was given as scheduled, and no fever was reported after the second dose.

Non-fatal SAEs are detailed in Table 30 in Section 13.1.

8.5. Medically attended adverse events

Overall, at least one unsolicited MAE up to the Day 180 phone contact was reported for 156 (52.2%) and 156 (51.7%) subjects in the Q-QIV group and D-TIV-YB group, respectively. Nasopharyngitis (27.1% and 25.5% of subjects, respectively), diarrhoea (8.0% and 9.6% of subjects, respectively) and pharyngitis (5.7% and 2.6% of subjects, respectively) were the only unsolicited MAEs reported by more than 5.0% of subjects in any study group.

MAE results are detailed in Table 24 to Table 26.

8.6. Adverse events leading to premature discontinuation of study vaccine and/or study

No (S)AEs leading to premature discontinuation of study vaccine were reported in this study from Day 0 up to the Day 180 phone contact.

8.7. Other significant adverse events

8.7.1. Potential immune-mediated diseases

During the entire study period, no pIMDs were reported for the subjects in the Q-QIV group. Two cases of pIMDs (alopecia areata and colitis ulcerative) were reported in the D-TIV-YB group. All reported pIMDs resolved by the end of the study (Day 180 phone contact). The pIMD Summary Table is presented in Section 13.2.

pIMDs results are detailed in Table 27 to Table 29.

8.8. Concomitant medications /vaccinations

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for detailed information.

8.9. Safety summary

A descriptive summary of safety data is provided in this section. These data, together with the safety data from other studies will contribute to the safety evaluation of the product.

Refer to the FLU-Q-QIV-013 (Day 56) Amendment 1 study report for the Day 56 summary of safety data.

For the Day 180 analysis:

- Overall, at least one unsolicited MAE up to the Day 180 phone contact was reported for 156 (52.2%) and 156 (51.7%) subjects in the Q-QIV group and D-TIV-YB group, respectively. Nasopharyngitis (27.1% and 25.5% of subjects, respectively), diarrhoea (8.0% and 9.6% of subjects, respectively) and pharyngitis (5.7% and 2.6% of subjects, respectively) were the only unsolicited MAEs reported by more than 5.0% of subjects in any study group.
- During the entire study period (from Day 0 up to the Day 180 phone contact), a total of 25 non-fatal SAEs were reported for 17 subjects. SAEs were reported for nine (3.0%) and eight (2.6%) subjects in the Q-QIV group and D-TIV-YB group, respectively. One of the SAEs reported in the Q-QIV group at the day of the vaccination (febrile convulsion) was considered by the investigator as related to the study vaccination, and resolved on the same day. All reported SAEs resolved by the end of the study (Day 180 phone contact).
- No fatal SAEs were reported during the study up to Day 180.
- No subject withdrew due to an AE or SAE from Day 0 up to the Day 180 phone contact.
- During the entire study period, no pIMDs were reported for the subjects in the Q-QIV group. Two cases of pIMDs (alopecia areata and colitis ulcerative) were

reported, both in the D-TIV-YB group. All reported pIMDs resolved by the end of the study (Day 180 phone contact).

9. OVERALL CONCLUSIONS

The following conclusions can be made based on the study safety results:

- At least one unsolicited MAE was reported for 156 (52.2%) and 156 (51.7%) subjects in the Q-QIV group and D-TIV-YB group, respectively. Nasopharyngitis (27.1% and 25.5% of subjects, respectively), diarrhoea (8.0% and 9.6% of subjects, respectively) and pharyngitis (5.7% and 2.6% of subjects, respectively) were the only MAEs reported by more than 5.0% of subjects in any study group.
- SAEs were reported for nine (3.0%) and eight (2.6%) subjects in the Q-QIV group and D-TIV-YB group, respectively. One of the SAEs reported in the Q-QIV group at the day of the vaccination (febrile convulsion) was considered by the investigator as related to the study vaccination, and resolved on the same day. No fatal SAEs were reported.
- Two cases of pIMDs (alopecia areata and colitis ulcerative) were reported, both in the D-TIV-YB group.

10. TABLES

10.1. Demographic characteristics

Table 16 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal (Total Vaccinated cohort)

	Q-QIV	D-TIV-YB	Total
Number of subjects vaccinated	299	302	601
Number of subjects completed	287	294	581
Number of subjects withdrawn	12	8	20
Reasons for withdrawal :			
Serious Adverse Event	0	0	0
Non-Serious Adverse Event	0	0	0
Protocol violation	0	0	0
Consent withdrawal (not due to an adverse event)	6	6	12
Migrated/moved from study area	2	1	3
Lost to follow-up (subjects with incomplete vaccination course)	3	1	4
Lost to follow-up (subjects with complete vaccination course)	1	0	1
Sponsor study termination	0	0	0
Others	0	0	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last visit

Table 17 Number of subjects at each visit and list of withdrawn subjects (Total Vaccinated cohort)

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
Q-QIV	VISIT 1 DAY 0	299		
			(b) (6)	Consent withdrawal, not due to an adverse event
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Migrated / moved from the study area
				Consent withdrawal, not due to an adverse event
	VISIT 2 DAY 28	290		
				Lost to follow-up
				Consent withdrawal, not due to an adverse event
				Migrated / moved from the study area
	VISIT 3 DAY 56	274		
	CONTACT DAY 180	287		
D-TIV-YB	VISIT 1 DAY 0	302		
				Lost to follow-up
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
	VISIT 2 DAY 28	296		
				Migrated / moved from the study area
				Consent withdrawal, not due to an adverse event
	VISIT 3 DAY 56	279		
	CONTACT DAY 180	294		
All	VISIT 1 DAY 0	601		
				Consent withdrawal, not due to an adverse event
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Migrated / moved from the study area
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
	VISIT 2 DAY 28	586		
				Lost to follow-up
				Migrated / moved from the study area
				Consent withdrawal, not due to an adverse event
				Migrated / moved from the study area
				Consent withdrawal, not due to an adverse event

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
	VISIT 3 DAY 56	553		
	CONTACT DAY 180	581		

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = number of subjects in each vaccine group
Withdrawn = number of subjects who did not come for the last visit

Table 18 Deviations from specifications between study visits for primed subjects (ESFU visit) (Total Vaccinated cohort)

		Dose:1-PI(D180)
Group		Protocol
		from 166 to 201 days
Q-QIV	N	13
	n	0
	%	0.0
	range	170 to 194
D-TIV-YB	N	15
	n	1
	%	6.7
	range	168 to 207
All	N	28
	n	1
	%	3.6
	range	168 to 207

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for intervals

Table 19 Deviations from specifications between study visits for unprimed subjects (ESFU visit) (Total Vaccinated cohort)

		Dose:1-PII(D180)
Group		Protocol
		from 166 to 201 days
Q-QIV	N	274
	n	1
	%	0.4
	range	166 to 208
D-TIV-YB	N	279
	n	0
	%	0.0
	range	166 to 195
All	N	553
	n	1
	%	0.2
	range	166 to 208

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for intervals

Table 20 Minimum and maximum activity dates (Total Vaccinated cohort)

Group	Activity number	Activity Description	Minimum date	Maximum date
Q-QIV	10	VISIT 1 DAY 0	01NOV2012	11DEC2012
Q-QIV	20	VISIT 2 DAY 28	28NOV2012	17JAN2013
Q-QIV	30	VISIT 3 DAY 56	27DEC2012	18FEB2013
Q-QIV	40	CONTACT DAY 180	23APR2013	19JUN2013
D-TIV-YB	10	VISIT 1 DAY 0	01NOV2012	11DEC2012
D-TIV-YB	20	VISIT 2 DAY 28	28NOV2012	17JAN2013
D-TIV-YB	30	VISIT 3 DAY 56	27DEC2012	21FEB2013
D-TIV-YB	40	CONTACT DAY 180	23APR2013	17JUN2013

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine

10.2. Safety results

Table 21 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term during the entire follow-up period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		9	3.0	1.4	5.6	8	2.6	1.2	5.2
Gastrointestinal disorders (10017947)	Colitis ulcerative (10009900)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Diarrhoea (10012735)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Intestinal obstruction (10022687)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Infections and infestations (10021881)	Amoebic dysentery (10001986)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Bacterial pyelonephritis (10059517)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Blastocystis infection (10005092)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Bronchiolitis (10006448)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Dengue fever (10012310)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Otitis media acute (10033079)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Peritonitis (10034674)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Pharyngitis streptococcal (10034839)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Rotavirus infection (10067470)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Septic shock (10040070)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Tonsillitis (10044008)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Bronchial hyperreactivity (10066091)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Pneumonia aspiration (10035669)	1	0.3	0.0	1.8	0	0.0	0.0	1.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 22 Percentage of doses with serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term during the entire follow-up period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		9	1.6	0.7	2.9	9	1.5	0.7	2.9
Gastrointestinal disorders (10017947)	Colitis ulcerative (10009900)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Diarrhoea (10012735)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Intestinal obstruction (10022687)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Infections and infestations (10021881)	Amoebic dysentery (10001986)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Bacterial pyelonephritis (10059517)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Blastocystis infection (10005092)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Bronchiolitis (10006448)	0	0.0	0.0	0.6	3	0.5	0.1	1.5
	Dengue fever (10012310)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Otitis media acute (10033079)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Peritonitis (10034674)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Pharyngitis streptococcal (10034839)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Rotavirus infection (10067470)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Septic shock (10040070)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Tonsillitis (10044008)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Bronchial hyperreactivity (10066091)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Pneumonia aspiration (10035669)	1	0.2	0.0	1.0	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 23 Global Summary of serious adverse events reported during the entire follow-up period (Total Vaccinated cohort)

	Group		
	Q-QIV	**D-TIV-YB**	**Total**
Number of subjects with at least one SAE reported	9	8	17
Number of doses followed by at least one SAE	9	9	18
Number of SAEs classified by MedDRA Preferred Term*	9	16	25
Number of SAEs reported**	9	16	25

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 24 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, during the entire follow-up period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		156	52.2	46.3	58.0	156	51.7	45.9	57.4
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Splenomegaly (10041660)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Tympanic membrane hyperaemia (10052154)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Eye disorders (10015919)	Conjunctivitis (10010741)	6	2.0	0.7	4.3	1	0.3	0.0	1.8
Gastrointestinal disorders (10017947)	Colitis ulcerative (10009900)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Diarrhoea (10012735)	24	8.0	5.2	11.7	29	9.6	6.5	13.5
	Diarrhoea haemorrhagic (10012741)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Gastrointestinal disorder (10017944)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Gingival bleeding (10018276)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Gingival swelling (10018291)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Intestinal obstruction (10022687)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Stomatitis (10042128)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Teething (10043183)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Vomiting (10047700)	3	1.0	0.2	2.9	2	0.7	0.1	2.4
General disorders and administration site conditions (10018065)	Oedema peripheral (10030124)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Pyrexia (10037660)	6	2.0	0.7	4.3	1	0.3	0.0	1.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Milk allergy (10027633)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Acute sinusitis (10001076)	5	1.7	0.5	3.9	5	1.7	0.5	3.8
	Acute tonsillitis (10001093)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Amoebic dysentery (10001986)	1	0.3	0.0	1.8	7	2.3	0.9	4.7
	Ascariasis (10003442)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Bacterial pyelonephritis (10059517)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Blastocystis infection (10005092)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Bronchiolitis (10006448)	5	1.7	0.5	3.9	5	1.7	0.5	3.8
	Bronchitis (10006451)	2	0.7	0.1	2.4	6	2.0	0.7	4.3
	Bronchopneumonia (10006469)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Bullous impetigo (10006563)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Candidiasis (10007152)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Cellulitis (10007882)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Conjunctivitis bacterial (10061784)	1	0.3	0.0	1.8	3	1.0	0.2	2.9
	Conjunctivitis infective (10010742)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Croup infectious (10011416)	3	1.0	0.2	2.9	1	0.3	0.0	1.8
	Cutaneous larva migrans (10059547)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Dengue fever (10012310)	2	0.7	0.1	2.4	0	0.0	0.0	1.2
	Dysentery (10051402)	0	0.0	0.0	1.2	3	1.0	0.2	2.9
	Ear infection (10014011)	10	3.3	1.6	6.1	10	3.3	1.6	6.0
	Eye infection viral (10015940)	0	0.0	0.0	1.2	1	0.3	0.0	1.8

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Fungal skin infection (10017543)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Gastroenteritis (10017888)	10	3.3	1.6	6.1	8	2.6	1.2	5.2
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Gastroenteritis viral (10017918)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Gingivitis (10018292)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Hordeolum (10020377)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Impetigo (10021531)	3	1.0	0.2	2.9	2	0.7	0.1	2.4
	Infection parasitic (10021857)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Influenza (10022000)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Injection site cellulitis (10050057)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Laryngitis (10023874)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Localised infection (10024774)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Lung infection (10061229)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Nasopharyngitis (10028810)	81	27.1	22.1	32.5	77	25.5	20.7	30.8
	Otitis media (10033078)	4	1.3	0.4	3.4	9	3.0	1.4	5.6
	Otitis media acute (10033079)	6	2.0	0.7	4.3	5	1.7	0.5	3.8
	Parasitic gastroenteritis (10067720)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Peritonitis (10034674)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Pharyngitis (10034835)	17	5.7	3.3	8.9	8	2.6	1.2	5.2
	Pharyngitis streptococcal (10034839)	2	0.7	0.1	2.4	1	0.3	0.0	1.8
	Pneumonia (10035664)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Rhinitis (10039083)	2	0.7	0.1	2.4	5	1.7	0.5	3.8
	Roseola (10039222)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Rotavirus infection (10067470)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Scarlet fever (10039587)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Septic shock (10040070)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Sinusitis (10040753)	6	2.0	0.7	4.3	4	1.3	0.4	3.4
	Skin bacterial infection (10052891)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Tinea pedis (10043873)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Tonsillitis (10044008)	8	2.7	1.2	5.2	9	3.0	1.4	5.6
	Tooth abscess (10044016)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Tracheitis (10044302)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Tracheobronchitis (10044314)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Upper respiratory tract infection (10046306)	7	2.3	0.9	4.8	6	2.0	0.7	4.3
	Urinary tract infection (10046571)	2	0.7	0.1	2.4	0	0.0	0.0	1.2
	Varicella (10046980)	2	0.7	0.1	2.4	1	0.3	0.0	1.8
	Viral infection (10047461)	6	2.0	0.7	4.3	6	2.0	0.7	4.3
	Viral rash (10047476)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Viral upper respiratory tract infection (10047482)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Contusion (10050584)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Face injury (10050392)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Joint injury (10060820)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Laceration (10023572)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Limb injury (10061225)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Lip injury (10055082)	1	0.3	0.0	1.8	0	0.0	0.0	1.2

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Dehydration (10012174)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.2	7	2.3	0.9	4.7
	Bronchial hyperreactivity (10066091)	7	2.3	0.9	4.8	6	2.0	0.7	4.3
	Bronchospasm (10006482)	3	1.0	0.2	2.9	3	1.0	0.2	2.9
	Cough (10011224)	2	0.7	0.1	2.4	3	1.0	0.2	2.9
	Pneumonia aspiration (10035669)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Rhinitis allergic (10039085)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Wheezing (10047924)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Skin and subcutaneous tissue disorders (10040785)	Alopecia areata (10001761)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Dermatitis diaper (10012444)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Dermatosis (10048768)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Eczema (10014184)	1	0.3	0.0	1.8	3	1.0	0.2	2.9
	Onychoclasis (10048886)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Prurigo (10037083)	3	1.0	0.2	2.9	3	1.0	0.2	2.9
	Rash (10037844)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Swelling face (10042682)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Urticaria (10046735)	5	1.7	0.5	3.9	2	0.7	0.1	2.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 25 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, during the entire follow-up period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		186	32.3	28.5	36.3	188	32.2	28.5	36.2
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Splenomegaly (10041660)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Tympanic membrane hyperaemia (10052154)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Eye disorders (10015919)	Conjunctivitis (10010741)	6	1.0	0.4	2.3	1	0.2	0.0	1.0
Gastrointestinal disorders (10017947)	Colitis ulcerative (10009900)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Diarrhoea (10012735)	25	4.3	2.8	6.3	32	5.5	3.8	7.7
	Diarrhoea haemorrhagic (10012741)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gastrointestinal disorder (10017944)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Gingival bleeding (10018276)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gingival swelling (10018291)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Intestinal obstruction (10022687)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Stomatitis (10042128)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
	Teething (10043183)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Vomiting (10047700)	3	0.5	0.1	1.5	2	0.3	0.0	1.2
General disorders and administration site conditions (10018065)	Oedema peripheral (10030124)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Pyrexia (10037660)	6	1.0	0.4	2.3	1	0.2	0.0	1.0
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Milk allergy (10027633)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Acute sinusitis (10001076)	5	0.9	0.3	2.0	5	0.9	0.3	2.0
	Acute tonsillitis (10001093)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
	Amoebic dysentery (10001986)	1	0.2	0.0	1.0	7	1.2	0.5	2.5
	Ascariasis (10003442)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Bacterial pyelonephritis (10059517)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Blastocystis infection (10005092)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Bronchiolitis (10006448)	6	1.0	0.4	2.3	6	1.0	0.4	2.2
	Bronchitis (10006451)	2	0.3	0.0	1.2	6	1.0	0.4	2.2
	Bronchopneumonia (10006469)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Bullous impetigo (10006563)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Candidiasis (10007152)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Cellulitis (10007882)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Conjunctivitis bacterial (10061784)	1	0.2	0.0	1.0	3	0.5	0.1	1.5
	Conjunctivitis infective (10010742)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Croup infectious (10011416)	3	0.5	0.1	1.5	1	0.2	0.0	1.0
	Cutaneous larva migrans (10059547)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dengue fever (10012310)	2	0.3	0.0	1.2	0	0.0	0.0	0.6
	Dysentery (10051402)	0	0.0	0.0	0.6	3	0.5	0.1	1.5
	Ear infection (10014011)	10	1.7	0.8	3.2	11	1.9	0.9	3.4
	Eye infection viral (10015940)	0	0.0	0.0	0.6	1	0.2	0.0	1.0

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Fungal skin infection (10017543)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Gastroenteritis (10017888)	10	1.7	0.8	3.2	8	1.4	0.6	2.7
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Gastroenteritis viral (10017918)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Gingivitis (10018292)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Hordeolum (10020377)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Impetigo (10021531)	3	0.5	0.1	1.5	2	0.3	0.0	1.2
	Infection parasitic (10021857)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Influenza (10022000)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Injection site cellulitis (10050057)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Laryngitis (10023874)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Localised infection (10024774)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Lung infection (10061229)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Nasopharyngitis (10028810)	88	15.3	12.4	18.5	89	15.3	12.4	18.4
	Otitis media (10033078)	4	0.7	0.2	1.8	9	1.5	0.7	2.9
	Otitis media acute (10033079)	6	1.0	0.4	2.3	6	1.0	0.4	2.2
	Parasitic gastroenteritis (10067720)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Peritonitis (10034674)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Pharyngitis (10034835)	19	3.3	2.0	5.1	8	1.4	0.6	2.7
	Pharyngitis streptococcal (10034839)	2	0.3	0.0	1.2	1	0.2	0.0	1.0
	Pneumonia (10035664)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Rhinitis (10039083)	2	0.3	0.0	1.2	5	0.9	0.3	2.0
	Roseola (10039222)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rotavirus infection (10067470)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Scarlet fever (10039587)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Septic shock (10040070)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Sinusitis (10040753)	6	1.0	0.4	2.3	4	0.7	0.2	1.7
	Skin bacterial infection (10052891)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Tinea pedis (10043873)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Tonsillitis (10044008)	8	1.4	0.6	2.7	9	1.5	0.7	2.9
	Tooth abscess (10044016)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Tracheitis (10044302)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Tracheobronchitis (10044314)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Upper respiratory tract infection (10046306)	7	1.2	0.5	2.5	6	1.0	0.4	2.2
	Urinary tract infection (10046571)	2	0.3	0.0	1.2	0	0.0	0.0	0.6
	Varicella (10046980)	2	0.3	0.0	1.2	1	0.2	0.0	1.0
	Viral infection (10047461)	6	1.0	0.4	2.3	6	1.0	0.4	2.2
	Viral rash (10047476)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Viral upper respiratory tract infection (10047482)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Contusion (10050584)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Face injury (10050392)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Joint injury (10060820)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Laceration (10023572)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Limb injury (10061225)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Lip injury (10055082)	1	0.2	0.0	1.0	0	0.0	0.0	0.6

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Dehydration (10012174)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.6	8	1.4	0.6	2.7
	Bronchial hyperreactivity (10066091)	7	1.2	0.5	2.5	6	1.0	0.4	2.2
	Bronchospasm (10006482)	3	0.5	0.1	1.5	3	0.5	0.1	1.5
	Cough (10011224)	2	0.3	0.0	1.2	3	0.5	0.1	1.5
	Pneumonia aspiration (10035669)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rhinitis allergic (10039085)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Wheezing (10047924)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Skin and subcutaneous tissue disorders (10040785)	Alopecia areata (10001761)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Dermatitis diaper (10012444)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
	Dermatosis (10048768)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Eczema (10014184)	1	0.2	0.0	1.0	3	0.5	0.1	1.5
	Onychoclasis (10048886)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Prurigo (10037083)	3	0.5	0.1	1.5	4	0.7	0.2	1.7
	Rash (10037844)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
	Swelling face (10042682)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Urticaria (10046735)	5	0.9	0.3	2.0	2	0.3	0.0	1.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 26 Global Summary of medically attended events reported during the entire follow-up period (Total Vaccinated cohort)

	Group		
	Q-QIV	**D-TIV-YB**	**Total**
Number of subjects with at least one MAE reported	156	156	312
Number of doses followed by at least one MAE	186	188	374
Number of MAEs classified by MedDRA Preferred Term*	302	312	614
Number of MAEs reported**	326	325	651

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 27 Percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire follow-up period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		0	0.0	0.0	1.2	2	0.7	0.1	2.4
Gastrointestinal disorders (10017947)	Colitis ulcerative (10009900)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Skin and subcutaneous tissue disorders (10040785)	Alopecia areata (10001761)	0	0.0	0.0	1.2	1	0.3	0.0	1.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 28 Percentage of doses with potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire follow-up period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		0	0.0	0.0	0.6	2	0.3	0.0	1.2
Gastrointestinal disorders (10017947)	Colitis ulcerative (10009900)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Skin and subcutaneous tissue disorders (10040785)	Alopecia areata (10001761)	0	0.0	0.0	0.6	1	0.2	0.0	1.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 29 Global Summary of potential immune-mediated diseases (pIMDs) reported during the entire follow-up period (Total Vaccinated cohort)

	Group		
	Q-QIV	**D-TIV-YB**	**Total**
Number of subjects with at least one pIMD reported	0	2	2
Number of doses followed by at least one pIMD	0	2	2
Number of pIMDs classified by MedDRA Preferred Term*	0	2	2
Number of pIMDs reported**	0	2	2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

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12. STUDY REPORT AUTHORS /CONTRIBUTING AUTHORS

Scientific Writer: (b) (6), contractor for GSK Biologicals

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Central Safety Contact: (b) (6), MD

Clinical Research & Development Lead (CRDL): (b) (6), MD PhD

Clinical Regulatory Affairs: (b) (6)

N + 1 equivalent of CRDL: (b) (6), MD

13. SERIOUS ADVERSE EVENTS / OTHER SIGNIFICANT ADVERSE EVENTS

13.1. SAE Listing

Table 30 Listing of SAEs reported during the entire follow-up period (Total Vaccinated cohort)

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
Q-QIV	(b) (6)		15	F	Dehydration	Dehydration	Metabolism and nutrition disorders	HO	2	37	5	2	N	Recovered / resolved
			12	M	Entrerococcus pyelonephitis	Bacterial pyelonephritis	Infections and infestations	HO	2	57	12	3	N	Recovered / resolved
			19	F	Streptococcus pharyngitis group a	Pharyngitis streptococcal	Infections and infestations	HO	2	32	11	3	N	Recovered / resolved
			30	M	Dengue	Dengue fever	Infections and infestations	HO	2	63	8	2	N	Recovered / resolved
			13	M	Pneumonia by immersion	Pneumonia aspiration	Respiratory, thoracic and mediastinal disorders	HO	2	59	8	3	N	Recovered / resolved
			16	M	Acute diahrrea	Diarrhoea	Gastrointestinal disorders	HO	2	3	7	2	N	Recovered / resolved
			10	M	Intestinal amebiasis	Amoebic dysentery	Infections and infestations	HO	2	89	9	2	N	Recovered / resolved
			17	F	Rotavirus disease	Rotavirus infection	Infections and infestations	HO	2	81	11	2	N	Recovered / resolved
			18	M	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	0	1	1	Y	Recovered / resolved
D-TIV-YB			10	M	Rsv bronchiolitis	Respiratory syncytial virus bronchiolitis	Infections and infestations	HO	2	63	21	2	N	Recovered / resolved
			16	M	Dehydration	Dehydration	Metabolism and nutrition disorders	HO	2	87	4	2	N	Recovered / resolved
			16		Right acute otitis media	Otitis media acute	Infections and infestations	HO	2	87	13	2	N	Recovered / resolved
			16		Tonsillitis	Tonsillitis	Infections and infestations	HO	2	87	13	2	N	Recovered / resolved

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
	(b) (6)		18	M	Asthma	Asthma	Respiratory, thoracic and mediastinal disorders	HO	2	33	3	3	N	Recovered / resolved
			18		Reactive airway disease	Bronchial hyperreactivity	Respiratory, thoracic and mediastinal disorders	HO	2	33	3	3	N	Recovered / resolved
			13	M	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	22	5	2	N	Recovered / resolved
			24	F	Rotavirus gastroenteritis	Gastroenteritis rotavirus	Infections and infestations	HO	2	92	6	2	N	Recovered / resolved
			10	M	Blastocystis hominis diarrhea	Blastocystis infection	Infections and infestations	HO	1	23	5	2	N	Recovered / resolved
			10		Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	23	12	2	N	Recovered / resolved
			16	M	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	2	148	12	2	N	Recovered / resolved
			17	M	Rotavirus gastroenteritis	Gastroenteritis rotavirus	Infections and infestations	HO	2	83	4	2	N	Recovered / resolved
			24	F	Ulcerative colitis perforated	Colitis ulcerative	Gastrointestinal disorders	HO	2	153	1	3	N	Recovered / resolved
			24		Partial intestinal obstruction	Intestinal obstruction	Gastrointestinal disorders	ER	2	151	3	3	N	Recovered / resolved
			24		Peritonitis	Peritonitis	Infections and infestations	HO	2	153	6	3	N	Recovered / resolved
			24		Septic shock	Septic shock	Infections and infestations	HO	2	151	22	3	N	Recovered / resolved

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
MED = Medically attended visit

13.2. Potential Immune-Mediated Diseases listing

Table 31 Listing of potential Immune-Mediated Disease reported during the entire follow-up period (Total Vaccinated cohort)

Group	Patient ID	Country	Age at onset (M)	Gender	Race	Primary System Organ Class	Preferred term	Dose	Day of onset	Relation	Serious pIMD based on Investigator?
D-TIV-YB	(b) (6)	Canada	38	Female	ASIAN - CENTRAL / SOUTH ASIAN HERITAGE	Skin and subcutaneous tissue disorders	Alopecia areata	2	65	N	N
		Honduras	24	Female	OTHER: HISPANIC	Gastrointestinal disorders	Colitis ulcerative	2	153	N	N

Group	Patient ID	SAE (Y/N)	Outcome	pIMD Source	MED type	Duration	Intensity
D-TIV-YB	(b) (6)	N	Recovered / resolved	MedDRA and investigator	MD	93	Mild
		Y	Recovered / resolved	MedDRA	HO	1	Severe

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
MED = Medically attended visit

13.3. CIOMS reports

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No: 2013-003155-38

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Honduras	(b) (6)		M	(b) (6)

7. & 13. DESCRIBE EVENT(S)

Febrile convulsion

This male subject was enrolled in the prophylactic double-blind study 116926 (FLU Q-QIV-013).
On (b) (6) he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

This subject received Flu Q-QIV.

On (b) (6) six hours after the 1st dose of Blinded vaccine, this 18-month-old subject developed febrile seizure. The event was clinically significant (or requiring intervention). The subject was treated with dipyrone. The event resolved on (b) (6) (b) (6) The investigator considered that there was a reasonable possibility that the febrile seizure may have been caused by investigational product and that the event was possibly due to

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Flu Quadrivalent split without adjuvant Quebec Injection (INFLUENZA VIRUS VAC polyv) GlaxoSmithKline

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADMINISTRATION
Unknown	Intramuscular

17. INDICATION(S) FOR USE: Unknown

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

14. IDENTIFIED DRUG(S)

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ N/A

15. DAILY/CUMULATIVE DOSE	16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0024955A

24c. DATE RECEIVED	DATE OF REPORT
14AUG2013	23SEP2013

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☒ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

study participation.

Investigator Comments : Narrative: for instructions o f Medical Comision of Central G S K that change this Adverse event non serious to S A E . The reason is regulatory agency has always been very sensitive about febrile seizure cases in pediatrics subjects and GSK has been explicitly asked to track the number of febrile seizure cases in the R M P (Risk Management Plan). Due to reason, convulsion was listed as a condition that should be considered as potential SAE in section 8.1.2 of the Q-QIV-013 protocol.With regard to the question of the reasonable possibility that the event might have been caused by the product in research is Yes, because a vaccine to be produced as expected adverse event, fever and a subject predisposed can present febrile seizure. In this case the seizure febrile was presented 6 hours post application of vaccine.
Event: Febrile seizure Start date: (b) (6) Outcome: resolved End Date: (b) (6)
Intensity: mild
Action taken with investigational product: NA
Is there reasonable possibility that the event may have been caused by investigational product: Yes.
This subject was attended only Emergency room, not hospitalized. No exam.Treatment: Only fever control with metamizol IM. This event not related with concomitans medication, or concomitant vaccines or prior medical condition. Subject is in good health.

GlaxoSmithKline Biologicals

Study title

Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) when administered in children.

Study detailed title

A Phase III, double-blind, randomised, controlled, multi-country, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to GSK Biologicals' trivalent influenza vaccine Fluarix™, administered intramuscularly to children 6 to 35 months of age.

Clinical Study Report for Study 116926 (FLU Q-QIV-013)

Development Phase III

Indication Studied: Immunisation against influenza in male and female subjects 6 to 35 months of age inclusive.

Study initiation date:	01-November-2012
Study completion date (For Day 56 Analysis):	21-February-2013
Data lock point (Date of database freeze) (For Day 56 Analysis):	15-April-2013
Date of report:	Amendment 1 Final 23-August-2013
Earlier Study Report:	Report Final 06-June-2013

Sponsor Signatory: Varsha K. Jain, MD
Director, Clinical Development Flu Vaccine
GlaxoSmithKline Biologicals

This study was performed in compliance with Good Clinical Practice including the archiving of essential documents.

GSK Biologicals' Study Report INS-BIO-CLIN-1010 v04

SYNOPSIS

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium** **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured **Name of active substance:** A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(for national authority only)**

Study No.: 116926 (FLU Q-QIV-013)

Title of the study: Immunogenicity and safety study of GlaxoSmithKline (GSK) Biologicals' quadrivalent (QIV) influenza vaccine (GSK2282512A) when administered in children.

Principal investigators:
This study was conducted by eight investigators in three countries (Canada, Dominican Republic and Honduras).

Study Centres:
Multi-centre study with six centres in Canada, one centre in Dominican Republic and one centre in Honduras.

Publication (reference): Not published as of 23-August-2013.

Study period: **Study initiation date:** 01-November-2012 **Study completion date (For Day 56 Analysis):** 21-February-2013 **Data lock point (Date of database freeze) (For Day 56 Analysis):** 15-April-2013	**Phase: III**

Indication: Immunisation against influenza in male and female subjects 6 to 35 months of age inclusive.

Treatment:
The study groups were as follows:

- Q-QIV: subjects received one dose (primed* subjects) of the FLU Q-QIV vaccine on Day 0 or two doses (unprimed** subjects) on Day 0 and Day 28
- D-TIV-YB: subjects received one dose (primed* subjects) of *Fluarix* on Day 0 or two doses (unprimed** subjects) on Day 0 and Day 28

*Primed subjects received two doses of a seasonal influenza vaccine separated by at least one month during the last season or at least one dose prior to the last season.
**Unprimed subjects did not receive any seasonal influenza vaccine in the past or only one dose for the first time in the last influenza season.

Objectives:
Primary:

- To assess the immunogenicity of FLU Q-QIV based on Center for Biologics Evaluation and Research (CBER)'s seroconversion rate (SCR) criterion for each of the four strains in children 6 to 35 months of age, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).
  Evaluation criterion:
  – The lower limit (LL) of the two-sided 95% confidence interval (CI) for SCR was to be ≥ 40% for each strain.
- To describe the reactogenicity of FLU Q-QIV and *Fluarix* in terms of solicited local and general adverse events (AEs), during a 7-day follow-up period.

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium** **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured **Name of active substance:** A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(for national authority only)**

Secondary:

- To test the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of geometric mean titre [GMT] and SCR) in all subjects approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively) by comparing FLU Q-QIV to *Fluarix.*
  Criteria to conclude superiority:
  Immunogenic superiority was to be concluded if:
  - The LL of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) was greater than 1.5, and
  - The LL of the two-sided 95% CI for the difference in SCR (FLU Q-QIV – *Fluarix*) was greater than 10%.
- To describe the immunogenicity (in terms of GMTs, seroprotection rates [SPRs], SCRs, and mean geometric increases [MGIs]) of FLU Q-QIV and *Fluarix*.
- To describe the safety of FLU Q-QIV and *Fluarix* in terms of:
  - Unsolicited AEs during the 28-day post-vaccination follow-up period (day of vaccination and 27 subsequent days).
  - Serious adverse events (SAEs), medically attended adverse events (MAEs), and potential immune-mediated diseases (pIMDs) during the entire study period*.
- To evaluate the relative risk of fever of FLU Q-QIV compared to *Fluarix* during a 4-day follow-up period.

*This clinical study report (CSR) includes safety information until 28 days post last vaccination. Safety information until the end of study will be described in an annex report.

Study design:
This was a Phase III, double-blind, randomised (1:1), controlled study with two parallel study groups to evaluate the immunogenicity and reactogenicity of FLU Q-QIV in children 6 to 35 months of age. Blood samples were collected on Day 0 and Day 28 for primed subjects, and on Day 0 and Day 56 for unprimed subjects.

Study vaccine, dose, mode of administration, lot no.:
Vaccination schedule /site:
One or two intramuscular (IM) injection(s) in the anterolateral side of left thigh (subjects < 12 months of age) or in the deltoid muscle of the non-dominant arm (subjects ≥ 12 months of age) on Day 0 (primed subjects) or Day 0 and Day 28 (unprimed subjects).
Vaccine composition /dose /lot number:
The quadrivalent influenza virus (FLU Q-QIV) candidate vaccine contained haemagglutinin (HA) from four influenza strains with a total of 60 µg (15 µg for each strain): A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Hubei-Wujiagang/158/09 (Yamagata lineage). The formulation was thimerosal-free. The total volume injected was 0.5 mL. The lot number was DFLHA760A.

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Reference vaccine /Comparator, dose and mode of administration, lot no.:
Vaccination schedule /site:
One or two IM injection(s) in the anterolateral side of left thigh (subjects < 12 months of age) or in the deltoid muscle of the non-dominant arm (subjects ≥ 12 months of age) on Day 0 (primed subjects) or Day 0 and Day 28 (unprimed subjects).
Vaccine composition /dose /lot number:
The trivalent control vaccine (D-TIV-YB), commercially available as *Fluarix*, contained HA from three influenza strains with a total of 45 µg (15µg for each strain): A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Hubei-Wujiagang/158/09 (Yamagata lineage). The formulation was thimerosal-free. The total volume injected was 0.5 mL. The lot number was AFLUA726A.

Study Population:
Healthy male or female infants between, and including, 6 and 35 months of age at the time of the first vaccination, without prior receipt of any seasonal or pandemic influenza vaccine within six months preceding the first dose of the study vaccine, or planned use during the study period, for whom the investigator believed that their parents/legally acceptable representatives (LARs) would comply with the requirements of the protocol. Written informed consent was obtained from the parents/LARs of each subject.

Duration of treatment: Approximately 3 to 5 weeks to complete enrolment and approximately 6 months for each enrolled subject to complete the study.

Primary Outcome/Efficacy Variables:
- Humoral immune response to each strain of FLU Q-QIV. Serum haemagglutination inhibition (HI) antibodies on Day 0 and 28 days after the last vaccine dose were used to calculate:
  - SCRs
- Solicited local and general AEs:
  - Occurrence of solicited local and general AEs (summarised by incidence rate, duration, intensity, and relationship to vaccination) during a 7-day follow-up period (i.e., day of vaccination and six subsequent days) after each vaccination in each group.

Secondary Outcome/Efficacy Variables:
- Serum anti-HA antibody titres against the four vaccine strains on Day 0 and 28 days after last vaccine dose were used to calculate:
  - GMTs
  - SCRs
  - SPRs
  - MGI
- Serum anti-HA antibody titres against B/Victoria strain 28 days after last vaccine dose were used to calculate:
  - GMT ratio (FLU Q-QIV/*Fluarix*)
  - SCR difference (FLU Q-QIV – *Fluarix*)

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER**	**(for national authority only)**
Name of finished product: GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Volume:**	
Name of active substance: A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**Page:**	

Secondary Outcome/Efficacy Variables, cont'd:

- Unsolicited AEs
  - Occurrence of unsolicited AEs (summarised by incidence rate, intensity, and relationship to vaccination) during a 28-day follow-up period (i.e., day of vaccination and 27 subsequent days) after each vaccination, in each group.
- MAEs, SAEs, and pIMDs:
  - Occurrence of MAEs, SAEs and pIMDs (summarised by incidence rate and relationship to vaccination) during the entire study period[*].
- Occurrence of any fever or Grade 3 or higher fever during a 4-day follow-up period after Dose 1 or Dose 2[**].

[*]Only safety information until 28 days post last vaccination was included in this CSR.
[**]Any fever is defined as ≥ 38.0°C and Grade 3 or higher fever as ≥ 39.0°C.

Statistical methods:

Analyses were performed as per protocol and per Statistical Analysis Plan (SAP).

Demography:

- Demographic characteristics (age, height, weight, gender and race) of each study vaccine group were tabulated. The mean age (in months) by gender of the vaccinated cohort, as a whole and by treatment group, was calculated.

Immunogenicity:

The analysis was based on the according-to-protocol (ATP) cohort for analysis of immunogenicity (primary analysis) and on the Total Vaccinated cohort (TVC) (complementary analysis).

- For the humoral immune response in terms of HI antibodies against all vaccine strains, GMTs, SCRs, SPRs and MGI were calculated with exact 95% CI at specified blood sampling time points for all subjects, each age strata and by priming status.
- To assess superiority, the GMT ratio of FLU Q-QIV over *Fluarix* and the two-sided 95% CI was calculated against the B/Brisbane/60/2008 like virus (Victoria) strain (Criterion for evaluation of superiority: LL of the two-sided 95% CI of the GMT ratio [FLU Q-QIV/*Fluarix*] > 1.5). In addition, difference of SCR (FLU Q-QIV minus *Fluarix*) and the 95% CI was calculated to assess superiority (Criterion for evaluation: LL of the two-sided 95% CI on the SCR difference [FLU Q-QIV - *Fluarix*] > 10%).

Safety:

The analysis was based on the TVC (primary analysis).

- Incidences of AEs (solicited local, solicited general and unsolicited), with 95% CI, were calculated for each treatment group and overall. The same tabulation was performed for Grade 3, related AEs and Grade 3 related AEs.
- MAEs, SAEs and pIMDs were collected and summarised until Day 56[*].
- The percentage of subjects reporting AEs resulting in a medically attended visit was tabulated.

[*]Until Day 56 for unprimed subjects and until Day 28 for primed subjects.

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Statistical methods, cont'd:

- Relative risk of subjects with any fever or Grade 3 or higher fever within 4 days of the vaccination(s) was calculated for all subjects and by age stratum, along with the 95% CI. As an exploratory analysis, relative risk of subjects with any or Grade 3 solicited AE during 7 days follow-up after vaccination(s) was calculated for all subjects and by age stratum, along with the 95% CI. Relative risk of subjects with any fever or Grade 3 or higher fever within 7 days or 48 hours of the vaccination(s) was calculated for all subjects and by age stratum, along with the 95% CI.

Synopsis Table 1: Study population (Total Vaccinated cohort)

Number of subjects	**Q-QIV**	**D-TIV-YB**	**Total**
Randomised, N (Total Vaccinated cohort)	299	302	601
Completed, n	286	294	580
Demographics	**Q-QIV**	**D-TIV-YB**	**Total**
N (Total Vaccinated cohort)	299	302	601
Females: Males (%)	51.8% : 48.2%	48.3% : 51.7%	50.1% : 49.9%
Mean Age, months (SD)	18.2 (8.17)	18.1 (8.34)	18.1 (8.25)

Q-QIV = FLU Q-QIV vaccine; D-TIV-YB = *Fluarix* vaccine; N = total number of subjects; n/% = number/percentage of subjects; SD = standard deviation

Summary:

This current report describes the main analysis which was performed when data on immunogenicity, reactogenicity and safety endpoints obtained up to and including Day 56 became available.

Immunogenicity:

Immunogenicity analysis was performed on the ATP cohort (primary analysis) and on the TVC (complementary analysis).

- The primary immunogenicity objective was met, as the LL of the two-sided 95% CI for SCR was ≥ 40% against all four strains (range 66.6% - 81.3%), approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).
- In addition, the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of GMT and SCR) was concluded (confirmatory secondary objective), as the LL of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) (5.32) was greater than 1.5, and the LL of the two-sided 95% CI for the difference in SCR (FLU Q-QIV – *Fluarix*) (57.65%) was greater than 10%.

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Synopsis Table 2: Seroconversion rate (SCR) for HI antibodies against the four vaccine strains 28 days after last vaccine dose (ATP cohort for immunogenicity)

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/California/7/2009 (H1N1)	Q-QIV	284	244	85.9	81.3	89.7
	D-TIV-YB	287	154	53.7	47.7	59.5
A/Victoria/361/2011 (H3N2)	Q-QIV	284	205	72.2	66.6	77.3
	D-TIV-YB	287	160	55.7	49.8	61.6
B/Hubei-Wujiagang/158/09	Q-QIV	284	224	78.9	73.7	83.5
	D-TIV-YB	287	222	77.4	72.1	82.1
B/Brisbane/60/2008	Q-QIV	284	210	73.9	68.4	79.0
	D-TIV-YB	287	28	9.8	6.6	13.8

Q-QIV = FLU Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4-fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Synopsis Table 3: Adjusted GMT ratios of HI antibody between FLU Q-QIV and D-TIV-YB for the B/Brisbane/60/2008 (Victoria) strain 28 days after last vaccine dose (ATP cohort for immunogenicity)

					Adjusted GMT ratio (Q-QIV / D-TIV-YB)		
	Q-QIV		D-TIV-YB			95% CI	
Antibody	**N**	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
B/Brisbane/60/2008 (1/DIL)	284	104.6	287	16.7	6.28	5.32	7.41

Q-QIV = FLU Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit; UL = upper limit

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Synopsis Table 4: Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the B/Brisbane/60/2008 (Victoria) strain 28 days after last vaccine dose (ATP cohort for immunogenicity)

							Difference in seroconversion rate (Q-QIV minus D-TIV-YB)		
	Q-QIV			D-TIV-YB				95% CI	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
B/Brisbane/60/2008 (1/DIL)	284	210	73.9	287	28	9.8	64.19	57.65	69.95

Q-QIV = FLU Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
Seroconversion rate defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at PII(D28)
For initially seropositive subjects : antibody titre at PII(D28) ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit; UL = upper limit

Synopsis Table 5: Summary of immunogenicity results (ATP cohort for immunogenicity)

Group	Timing	N	≥ 1:10				GMT			SPR				MGI		
			n	%	95% CI		Value	95% CI		n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL			LL	UL		LL	UL
A/California/7/2009 (H1N1)																
Q-QIV	PRE	284	60	21.1	16.5	26.3	9.6	8.1	11.3	46	16.2	12.1	21.0	-	-	-
	POST	284	276	97.2	94.5	98.8	157.1	132.8	185.9	254	89.4	85.3	92.8	16.4	14.3	18.7
D-TIV-YB	PRE	287	59	20.6	16.0	25.7	9.8	8.3	11.6	47	16.4	12.3	21.2	-	-	-
	POST	287	240	83.6	78.8	87.7	61.2	49.2	76.2	169	58.9	53.0	64.6	6.2	5.3	7.3
A/Victoria/361/2011 (H3N2)																
Q-QIV	PRE	284	101	35.6	30.0	41.4	17.4	14.1	21.5	93	32.7	27.3	38.5	-	-	-
	POST	284	275	96.8	94.1	98.5	159.4	129.4	196.3	231	81.3	76.3	85.7	9.1	8.0	10.5
D-TIV-YB	PRE	287	89	31.0	25.7	36.7	13.8	11.4	16.8	74	25.8	20.8	31.3	-	-	-
	POST	287	274	95.5	92.4	97.6	103.0	83.7	126.7	191	66.6	60.8	72.0	7.5	6.4	8.7
B/Hubei-Wujiagang/158/09																
Q-QIV	PRE	284	62	21.8	17.2	27.1	7.7	6.9	8.7	26	9.2	6.1	13.1	-	-	-
	POST	284	280	98.6	96.4	99.6	114.2	100.0	130.5	242	85.2	80.5	89.1	14.8	12.8	17.1
D-TIV-YB	PRE	287	58	20.2	15.7	25.3	7.2	6.5	8.0	24	8.4	5.4	12.2	-	-	-
	POST	287	280	97.6	95.0	99.0	107.2	92.2	124.6	229	79.8	74.7	84.3	14.8	12.8	17.2

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Group	Timing	N	≥ 1:10				GMT			SPR				MGI		
			n	%	95% CI		Value	95% CI		n	%	95% CI		Value	95% CI	
					LL	UL		LL	UL			LL	UL		LL	UL
B/Brisbane/60/2008																
Q-QIV	PRE	284	87	30.6	25.3	36.4	10.6	9.1	12.4	56	19.7	15.3	24.8	-	-	-
	POST	284	275	96.8	94.1	98.5	111.4	91.9	135.2	216	76.1	70.7	80.9	10.5	9.2	11.9
D-TIV-YB	PRE	287	73	25.4	20.5	30.9	9.3	8.0	10.7	45	15.7	11.7	20.4	-	-	-
	POST	287	153	53.3	47.4	59.2	15.6	13.3	18.5	74	25.8	20.8	31.3	1.7	1.5	1.9

Q-QIV = FLU Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
GMT = geometric mean antibody titre calculated on all subjects
SPR = seroprotection rate
MGI = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
For GMT, titres ≥ 1:10 and SPR:
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
For MGI:
N = number of subjects with pre- and post-vaccination results available
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE = Pre-vaccination at Visit Day 0
POST = Post-vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Safety /reactogenicity:

The safety analysis was performed on the TVC (primary analysis).

Overall incidence of AEs:

- During the 7-day post-vaccination period, at least one symptom (solicited and unsolicited) was reported for 63.5% and 67.9% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Among solicited symptoms, at least one local symptom was reported for 32.8% and 31.8% of subjects, respectively, and at least one general symptom was reported for 59.9% and 62.6% of subjects, respectively.

Solicited local and general AEs:

- Injection site pain was the most frequently reported solicited local AE (32.6% and 30.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively). Grade 3 injection site pain was reported for 7 (2.4%) and 3 (1.0%) subjects, respectively.
- Irritability/fussiness was the most frequently reported solicited general AE (40.7% and 41.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively). Grade 3 irritability/fussiness was reported for 5.2% and 4.7% of subjects, respectively.

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Unsolicited AEs:

- During the 28-day post-vaccination period, at least one unsolicited AE was reported for 47.5% and 54.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Nasopharyngitis (26.1% and 29.8% of subjects, respectively) and diarrhoea (12.7% and 12.6% of subjects, respectively) were the only two unsolicited AEs reported by more than 5.0% of subjects. Only for one subject in the Q-QIV group a Grade 3 unsolicited AE with causal relationship to vaccination was reported.

Serious adverse events:

- A total of four non-fatal SAEs were reported for three subjects during the entire study period until Day 56. None of these SAEs were considered related to the study vaccine in the opinion of the investigator.

Medically attended adverse events:

- At least one unsolicited AE with a medically attended visit up to Day 56 was reported for 32.4% and 33.4% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Nasopharyngitis (17.4% and 17.9% of subjects, respectively) and diarrhoea (6.0% and 7.3% of subjects, respectively) were the only two MAEs reported by more than 5.0% of subjects.

Withdrawals due to adverse events /serious adverse events:

- No subject withdrew due to an AE or SAE from Day 0 to Day 56.

Other safety parameters:

- No pIMDS were reported up to Day 56.
- The relative risk of any fever for Q-QIV compared to D-TIV-YB during a 4-day follow-up period was 1.12 with a 95% CI of [0.76; 1.64] (p-value = 0.6439). The relative risk of Grade 3 or higher fever for Q-QIV compared to D-TIV-YB during a 4-day follow-up period was 2.04 with a 95% CI of [0.91; 4.60] (p-value = 0.0977).

Important safety information received after the data lock point (database freeze date):

- One report of a potential immune-mediated disorder was received after the data lock point of this report. This report described a three year-old female who developed hair loss 65 days after the second blinded dose of vaccine. The subject was evaluated in the office one week later, and found to have an area of alopecia over the anterior part of the scalp. A diagnosis of alopecia areata was made, and the hair loss slowly improved within 4 weeks time, without any treatment. This pIMD was considered to be non-serious, and the investigator did not consider the event to be related to the investigational product. This late-breaking information does not change the safety profile of the data presented in this report.

Conclusion:

The following conclusions can be made based on the study results:

- The primary immunogenicity objective was met. For all four strains, the LL of the two-sided 95% CI for SCR was ≥ 40% (range 66.6% - 81.3%), approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium** **Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured **Name of active substance:** A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Hubei-Wujiagang/158/09 (Yamagata lineage)	**TABULAR FORMAT REFERRING TO PART OF THE DOSSIER** **Volume:** **Page:**	**(for national authority only)**

- During the 7-day post-vaccination period, at least one symptom (solicited and unsolicited) was reported for 63.5% and 67.9% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Injection site pain was the most frequently reported solicited local AE (32.6% and 30.6% of subjects, respectively) and irritability/fussiness the most frequently reported solicited general AE (40.7% and 41.6% of subjects, respectively).
- The secondary objective of immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of GMT and SCR) was also met. The LL of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) (5.32) was greater than 1.5 and the LL of the two-sided 95% CI for the difference in SCR (FLU Q-QIV - *Fluarix*) (57.65%) was greater than 10%.
- No other safety concerns were identified. The FLU Q-QIV and *Fluarix* vaccines were generally well tolerated.

References: Not applicable

Date of report: Amendment 1 Final: 23-August-2013

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LIST OF ABBREVIATIONS

AE	Adverse Event
ANCOVA	Analysis of Covariance
ATP	According-to-Protocol
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence Interval
CIOMS	Council for International Organisations of Medical Sciences
CRO	Contract Research Organisation
CSR	Clinical Study Report
eCRF	electronic Case Report Form
EMEA	European Medicines Agency
GCP	Good clinical practice
GMT	Geometric Mean Titre
GSK	GlaxoSmithKline
HA	Haemagglutinin
HI	Haemagglutination Inhibition
ICF	Informed Consent Form
IEC	Independent Ethics Committee
IM	Intramuscular
IRB	Institutional Review Board
LAR	Legally Acceptable Representative
LL	Lower Limit
MAE	Medically Attended Adverse Events
MedDRA	Medical Dictionary for Regulatory Activities
MGI	Mean Geometric Increase
pIMD	potential Immune-Mediated Disease
PT	Preferred Term
QIV	Quadrivalent
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Systems

SBIR	Randomisation System on Internet
SCR	Seroconversion Rate
SOP	Standard Operating Procedures
SPR	Seroprotection Rate
TIV	Trivalent
TVC	Total Vaccinated cohort
WHO	World Health Organisation

GLOSSARY OF TERMS

Adverse event (AE):	Any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An adverse event (AE) was therefore any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this included failure to produce expected benefits (i.e., lack of efficacy), abuse or misuse.
Blinding:	A procedure in which one or more parties to the trial are kept unaware of the treatment assignment in order to reduce the risk of biased study outcomes. The level of blinding is maintained throughout the conduct of the trial, and only when the data are cleaned to an acceptable level of quality will appropriate personnel be unblinded or when required in case of a serious adverse event (SAE). In a double blind study, the subject, the investigator and sponsor staff who are involved in the treatment or clinical evaluation of the subjects and the review or analysis of data are all unaware of the treatment assignment.
Child in care:	A child who has been placed under the control or protection of an agency, organisation, institution or entity by the courts, the government or a government body, acting in accordance with powers conferred on them by law or regulation. The definition of a child in care can include a child cared for by foster parents or living in a care home or institution, provided that the arrangement falls within the definition above. The definition of a child in care does not include a child who is adopted or has an appointed legal guardian.
Eligible:	Qualified for enrolment into the study based upon strict adherence to inclusion/exclusion criteria.
Epoch:	An epoch is a self-contained set of consecutive time points or a single time point from a single protocol. Self-contained means that data collected for all subjects at all time points within that epoch allows to draw a complete conclusion to define or precise the targeted label of the product. Typical examples of epochs are primary vaccinations, boosters, yearly immunogenicity follow-ups, and surveillance periods for efficacy or safety.

eTrack:	GlaxoSmithKline (GSK)'s tracking tool for clinical trials.
Evaluable:	Meeting all eligibility criteria, complying with the procedures defined in the protocol, and, therefore, included in the according-to-protocol (ATP) analysis (see Sections 5.6 and 5.10.4 for details on criteria for evaluability).
Geometric Mean Titre (GMT):	The anti-log of the mean of the log (base 10) transformed inverse titres (the number X would denote the inverse of a titre expressed as "1:X"). Antibody titres below the cut-off of the assay are given an arbitrary value of half the cut-off for the purpose of GMT calculation.
Immunological correlate of protection:	The defined humoral antibody response above which there is a high likelihood of protection in the absence of any host factors that might increase susceptibility to the infectious agent.
Investigational vaccine/product: **(Synonym of Investigational Medicinal Product)**	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Mean Geometric Increase (MGI):	MGI is defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal haemagglutination inhibition (HI) titre to the pre-vaccination (Day 0) reciprocal HI titre.
Potential Immune-Mediated Disease (pIMDs):	Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.
Primary completion date:	The date that the final subject was examined or received an intervention for the purpose of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.
Primed subjects:	All subjects who have received two doses of seasonal influenza vaccine separated by at least one month during the last season or have received at least one dose prior to last season.
Randomisation:	The process of assigning trial subjects to study material pertaining to groups using an element of chance to determine the assignments in order to reduce bias.

Self-contained study:	Study with objectives not linked to the data of another study.
Serious Adverse Event (SAE):	Any untoward medical occurrence in a patient or clinical investigation subject that: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.
Seroconversion Rate (SCR):	SCR is defined as the proportion of vaccinees who have either a pre-vaccination titre < 1:10 and a postvaccination titre ≥ 1:40 or a pre-vaccination titre ≥ 1:10 and at least a four-fold increase in post-vaccination titre.
Seroprotection Rate (SPR):	The seroprotection rate or SPR is defined as the proportion of vaccinees with a serum HI titre ≥ 1:40.
Site Monitor:	An individual assigned by the sponsor who is responsible for assuring proper conduct of clinical studies at one or more investigational sites.
Solicited AE:	AEs to be recorded as endpoints in the clinical study. The presence/occurrence/intensity of these events is actively solicited from the subject or an observer during a specified post-vaccination follow-up period.
Sub-cohort:	A group of subjects for whom specific study procedures are planned as compared to other subjects
Subject:	Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the clinical study, either as a recipient of the vaccine(s)/product(s) or as a control.
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the study.
Treatment:	Term used throughout the clinical study to denote a set of investigational product(s) or marketed product(s) or placebo intended to be administered to a subject, identified by a unique number, according to the study randomisation or treatment allocation.
Treatment number:	A number identifying a treatment to a subject, according to the study randomisation or treatment allocation.
Unprimed subjects:	Subjects who have not received any seasonal influenza vaccine in the past or received only one dose for the first time in the last influenza season.

Unsolicited AE:	Any AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited AE .

TRADEMARKS

The following trademarks are used in the present report.

Note: In the body of the Study Report (including the synopsis), the names of the vaccines/products and/or medications will be written without the superscript symbol ™ or ® and in *italics*.

Trademarks of the GlaxoSmithKline group of companies	Generic description
FluarixTM	Inactivated trivalent split virion influenza vaccine

1. ETHICS

1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational centre Independent Ethics Committee (IEC) and Institutional Review Board (IRB).

1.2. Ethical conduct of the study

Overall, this study was conducted in accordance with "good clinical practice" (GCP) and all applicable regulatory requirements, including the Declaration of Helsinki.

During the course of the study, whenever potential issues with regard to the conduct of the study were identified, either via site monitoring activities or brought to GlaxoSmithKline (GSK) Biologicals' attention by other oversight mechanisms, these issues were investigated and appropriate corrective and/or preventive actions where possible were taken. Refer to Sections 5.11 and 6.2.3.

1.3. Subject information and consent

Written informed consent was obtained from each parent/Legally Acceptable Representative (LAR) prior to the performance of any study-specific procedures. Case report forms (CRFs) were provided for each subject's data to be recorded.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

2.1. Administrative structure

This study was conducted by eight investigators in three countries (Canada, Dominican Republic and Honduras).

GSK Biologicals was responsible for administration of the study, including clinical trial supply management and laboratory facilities for immunological testing.

Data management was performed by Keyrus, contractor for GSK Biologicals, Lasne, Belgium. Statistical analyses were performed by GSK Biologicals. Writing of the study protocol and clinical study report (CSR) was performed by Emtex, contractor for GSK Biologicals, Sint-Gillis-Waas, Belgium. Monitoring at the sites was performed by GSK Inc. Canada, Arka Servicios de Recursos Humanos S.A., Panama and GSK Panama. Immunological testing of serum samples was performed by GSK Biologicals at the Dresden site, Germany.

2.2. Clinical Study Report revision history

This Clinical Study Report (CSR) needed to be amended.

A typo error was noted in Synopsis Table 4 (Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the B/Brisbane/60/2008 [Victoria] strain 28 days after last vaccine dose [ATP cohort for immunogenicity]) after the main (D56) CSR was completed. In the column header, Q-QIV and D-TIV-YB were flipped, which gave the wrong impression that D-TIV-YB was superior to Q-QIV.

This change does not alter the study conclusions.

3. INTRODUCTION

Influenza is a serious public health problem; it has a high incidence in the human population and causes regular large-scale morbidity and mortality. During seasonal epidemics, 5-15% of the worldwide population is typically infected, resulting in 3-5 million cases of severe illness and a quarter to half a million excess deaths annually. Most deaths associated with influenza in industrialised countries occur among people 65 years of age or older [WHO, 2009], although infection is most common in children [O'Brien, 2004; Izurieta, 2000]. In particular, children younger than 5 years of age have incidence rates of severe influenza disease and hospitalisation due to influenza second only to the elderly population.

The highest influenza burden in terms of paediatric respiratory admissions is seen in infants 6 to 11 months of age [Schanzer, 2006] and rates of illness in children younger than 2 years of age are substantially higher than those in children 2 years of age or older [CDC, 2007; Poehling, 2006]. Children also play an important role in the spread of the disease [Brownstein, 2008], possibly because of their high levels of virus shedding. Since annual influenza vaccination is currently the most effective means of controlling influenza and preventing its complications and mortality [WHO, 2009], there is a general trend to extend the recommendation for influenza vaccinations not only to children at high risk of complicated influenza, but also to healthy children and adolescents. The effectiveness of influenza vaccination is, however, dependent on adequate matching between the circulating viruses and the viruses contained in the vaccine, the age of the child and the type of vaccine.

Since 1983, two antigenically distinct lineages of influenza B have circulated in the world. Their co-existence has also resulted in the emergence and subsequent worldwide circulation of a reassortant B virus possessing a Victoria-lineage haemagglutinin (HA) with a Yamagata-lineage derived neuraminidase [Barr, 2006]. In the United States, both Yamagata and Victoria lineages have co-circulated since the 2001-2002 influenza season.

Sera from adults vaccinated with the virus from one B lineage show some modest level of cross-reactivity against the other B lineage in vitro, which may be due to a prior natural exposure or vaccine priming [Barr, 2006; Heckler, 2007]. However, infants and children are much less likely to generate such a cross-reactive antibody response, presumably because of limited prior immunologic experience with influenza, and thus may be more susceptible than adults to infection with a co-circulating alternate lineage B strain. In

studies of unimmunised (unprimed) infants, no measurable cross-reactive antibodies to the alternate B lineage were found in the sera of naïve children after their first vaccine exposures [Hannoun, 2004; Heckler, 2007; Hobson, 1972]. Englund also showed that young children who have been exposed to prior priming manifested good boosting of influenza A responses, even when the vaccine virus has drifted somewhat from the original priming exposure. However, cross-lineage B virus priming was quite poor [Englund, 2006]. Sera from naïve ferrets (modelling young children) that are infected with a single B virus (and not exposed to other human influenza viruses), also show little or no cross-reactivity between the two B lineages [Barr, 2006].

From 2001 to 2009, influenza B viruses have accounted for 6.9% to 38.7% of clinical isolates from Centers for Disease Control (CDC) surveillance [CDC, 2010]. In 5 of these 8 years, a substantial proportion of B virus isolates have been representative of the genetic lineage not included in the trivalent (TIV) vaccine, and have accounted for 6.4% to 29.9% (median of 8.5%) of all influenza virus isolates [CDC, 2010].

The consequences of such a B virus mismatch could be severe. During the 2007-2008 season, almost 30% of influenza viruses tested at the CDC in the United States were type B, and 98% of them did not match the lineage contained in the TIV vaccine [CDC, 2008]. Assuming that a quadrivalent (QIV) vaccine containing a second B strain had been used in the 2007-2008 season rather than a TIV vaccine, a public health impact model for influenza-associated health outcomes estimated that the QIV seasonal vaccine could have prevented an additional 1090514 influenza cases, and resulted in 7488 fewer hospitalisations and 321 fewer deaths [Reed, 2009]. Because the two evolutionarily distinct lineages of influenza B virus continue to co-circulate, and cross-reactivity between the two lineages is low in the paediatric population (which has limited immunologic experience with influenza), an additional B strain antigen in the seasonal vaccine may offer greater efficacy and broader protection to children [Englund, 2006; Levandowski, 1991]. In addition, the 2007-2008 experience suggested that mismatched B virus morbidity was substantial in the elderly [Proff, 2009]; and these vulnerable persons could theoretically benefit from improved herd immunity resulting from immunisation of children as well as direct immunisation. These considerations have lead GSK Biologicals to develop a candidate QIV seasonal influenza vaccine, FLU Q-QIV (GSK2282512A), comprised of two A and two B strains.

Fluarix, formulated with two influenza A strains (A/H1N1 and A/H3N2) and one influenza B strain (Yamagata lineage B strain), is licensed for use in children 6 months of age and older in many countries. The Yamagata lineage B strain in Fluarix is the B strain recommended by the World Health Organisation (WHO) for the Northern Hemisphere 2012-2013 influenza season. The QIV vaccine, termed Q-QIV to indicate that it is manufactured at the Quebec site, is formulated with two influenza A strains (A/H1N1 and A/H3N2) and two influenza B strains (the same Yamagata lineage B strain as that in Fluarix, as well as a second Victoria lineage, B strain).

FLU Q-QIV has been studied in 300 children 6 to 35 months of age, given as a 0.5 mL dose in an open arm of the paediatric study, FLU Q-QIV-003. The 0.5 mL dose was well tolerated and immunogenic in children 6 to 35 months of age in this study, however no control vaccine was used. The primary purpose of this FLU Q-QIV-013 study was to

evaluate the immunogenicity and reactogenicity of Q-QIV with respect to a TIV control, Fluarix, in children 6 to 35 months of age.

4. STUDY OBJECTIVES

4.1. Primary objectives

- To assess the immunogenicity of FLU Q-QIV based on Center for Biologics Evaluation and Research (CBER)'s seroconversion rate (SCR) criterion for each of the four strains in children 6 to 35 months of age, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed* subjects, respectively).

  Evaluation criterion:

  – The lower limit (LL) of the two-sided 95% confidence interval (CI) for SCR was to be ≥ 40% for each strain.

  * See GLOSSARY OF TERMS for definitions of primed and unprimed subjects.

- To describe the reactogenicity of FLU Q-QIV and *Fluarix* in terms of solicited local and general adverse events (AEs), during a 7-day follow-up period.

See Section 5.10.1 for details of the primary endpoints. See Section 5.4.1 for the four strains included in the study vaccine.

4.2. Secondary objectives

- To test the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of geometric mean titre [GMT] and SCR) in all subjects approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively) by comparing FLU Q-QIV to *Fluarix*.

  Criteria to conclude superiority:

  Immunogenic superiority was to be concluded if:

  – The LL of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) was greater than 1.5, and

  – The LL of the two-sided 95% CI of the difference in SCR (FLU Q-QIV - *Fluarix*) was greater than 10%.

- To describe the immunogenicity (in terms of GMTs, seroprotection rates [SPRs], SCRs, and mean geometric increases [MGIs]) of FLU Q-QIV and *Fluarix*.

- To describe the safety of FLU Q-QIV and *Fluarix* in terms of:

  – Unsolicited AEs during the 28-day post-vaccination follow-up period (day of vaccination and 27 subsequent days).

  – Serious adverse events (SAEs), medically attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period.

- To evaluate the relative risk of fever of FLU Q-QIV compared to *Fluarix* during a 4-day follow-up period.

See Section 5.10.2 for details of the secondary endpoints.

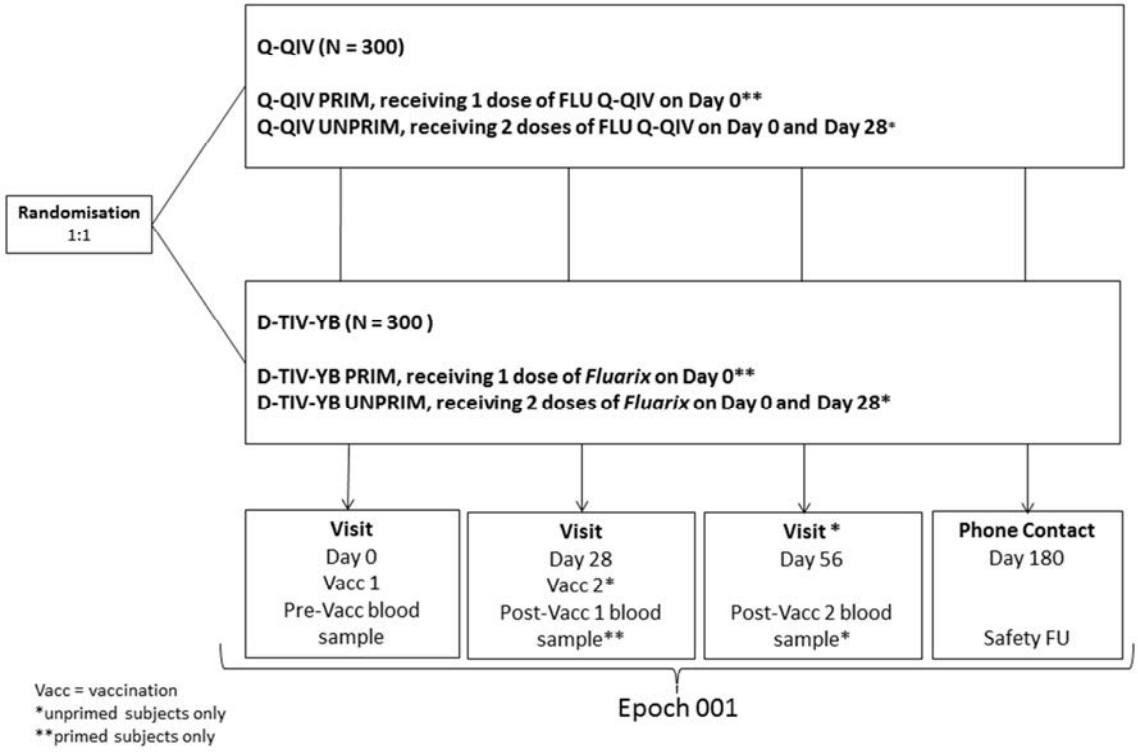
5. INVESTIGATIONAL PLAN

5.1. Study design

5.1.1. Overall study design – Description

Figure 1 provides a schematic overview of the study design.

Figure 1 Study design



- **Experimental design:** Phase III, double-blind, randomised, controlled, parallel-group, multi-centre, and multi-country study.
- **Duration of the study:** Approximately 3 to 5 weeks to complete enrolment and approximately 6 months for each enrolled subject to complete the study.
  - Epoch 001: Primary starting at Visit Day 0 and ending at Phone Contact Day 180.

- **Study groups:**

Table 1 Study groups and epochs foreseen in the study

Study Groups	Number of subjects	Age (Min – Max) (age unit)	Epochs
			Epoch 001
Q-QIV PRIM	300	6 months - 35 months	x
Q-QIV UNPRIM			
D-TIV-YB PRIM	300	6 months - 35 months	x
D-TIV-YB UNPRIM			

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine name	Study Groups			
		Q-QIV PRIM	Q-QIV UNPRIM	D-TIV-YB PRIM	D-TIV-YB UNPRIM
Q-QIV	FLU Q-QIV	x	x		
D-TIV-YB	*Fluarix*			x	x

- **Control:** active control (*Fluarix*)

- **Vaccination schedules:**

  – Primed* subjects (Q-QIV PRIM and D-TIV-YB PRIM): one intramuscular (IM) injection, on Day 0.

  – Unprimed* subjects (Q-QIV UNPRIM and D-TIV-YB UNPRIM): two IM injections, on Day 0 and Day 28.

  * See GLOSSARY OF TERMS for definitions of primed and unprimed subjects.

- **Treatment allocation**: Subjects were randomised 1:1 in the Q-QIV and D-TIV-YB groups.

  – Age (6 to 17 months, 18 to 35 months), study centre and the pre-study influenza priming status of the subjects were treated as minimisation factors to ensure equal representation of primed versus unprimed subjects, as well as equal representation of different age groups, and different centres in the two treatment groups.

- **Blinding**:

Table 3 Blinding of study epochs

Study Epochs	Blinding
Epoch 001	double-blind

Refer to Section 5.5 for details of unblinding.

- **Sampling schedule**: Blood samples were collected on Day 0 and Day 28 for primed subjects, and on Day 0 and Day 56 for unprimed subjects.

- **Type of study**: self-contained

- **Data collection**: electronic Case Report Form (eCRF)

5.1.2. Discussion of study design

This study was intended to generate controlled data of the FLU Q-QIV candidate vaccine in children 6 to 35 months of age. In particular, this study was designed to estimate the expected incidence of solicited AEs following administration of FLU Q-QIV in contrast to a licensed D-TIV (*Fluarix*) vaccine. Fever following vaccination was an objective measure of reactogenicity that was solicited. As fever following vaccination could be associated with febrile convulsions in this age group, the study's sample size was designed to afford a high probability to detect fever ≥ 38°C or fever ≥ 39°C. The group size (N = 300 per treatment) also permitted an exploratory subgroup analysis of responses by age (6 to 17 months, 18 to 35 months) (see Section 5.10.3).

Moreover, the sample size in this study when combined with supportive data from other completed controlled and uncontrolled studies of GSK's QIV formulations created a safety database of approximately 1000 subjects 6 to 35 months of age.

The control vaccine was *Fluarix* (D-TIV), which is licensed for use in children 6 months of age and older in many countries.

Effective immunisation was demonstrated by confirming that the SCR for each strain of the FLU Q-QIV candidate vaccine attained the CBER acceptance criterion (LL 95% CI ≥ 40%) [FDA, 2007]. As this study enrolled very young children, many of whom lacked a prior history of influenza vaccination or prior exposure to influenza A or B infection, it could be anticipated that the SCR was similar to the SPR. Consequently, although the SPR was described, the study's success did not require a demonstration that the SPR attained the CBER acceptance criterion (LL 95% CI ≥ 70%), as this criterion was developed for immunologically primed subjects. There was adequate power both to confirm acceptable immunogenicity and to demonstrate superiority to the control with respect to the immune response to the added B lineage omitted from the control vaccine.

Unprimed study participants received two 0.5 mL doses of FLU Q-QIV or *Fluarix* were administered IM at an approximate 28-day interval. Primed subjects received a single 0.5 mL dose of FLU Q-QIV or *Fluarix*. The 0.5 mL dose has been routinely recommended by the National Advisory Committee on Immunization (NACI) for children 6 to 35 months of age for inactivated seasonal flu vaccines since 2011.

5.2. Study procedures

5.2.1. Outline of study procedures

Table 4 and Table 5 summarise the list of study procedures during study visits and the final study contact for primed and unprimed subjects, respectively.

Table 4 List of study procedures for primed subjects – one vaccine dose

Age	6 to 35 months		
Epoch	Epoch 001		
Type of contact	visit	visit	phone contact
Time points	Day 0	Day 28	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	
Informed consent by parent(s)/LAR(s)	●		
Check inclusion/exclusion criteria	●		
Check elimination criteria (see Section 5.3.3)		●	●
Check contraindications to vaccination	●		
Collect demographic data (including weight and height)	●		
Medical history	●		
History of influenza vaccination	●		
Physical examination (history directed)	●	O §	
Pre-vaccination body temperature	●		
Internet randomisation	●		
Blood sampling (approximately 4 mL) for humoral immune response determination	●	●	
Vaccine administration	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily* (Days 0-6) and unsolicited AEs (Days 0-27)	O		
Return of diary cards		O	
Diary card transcription by investigator		●	
Record any concomitant medication/vaccination	●	●	●
Record any intercurrent medical conditions **	●	●	●
Recording of SAEs	● #	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●
Recording of MAEs and pIMDs	●	●	●
Study conclusion			●

Vacc = vaccination; pIMDs = potential Immune-Mediated Diseases; LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; SAE = Serious Adverse Event

● used to indicate a study procedure that required documentation in the individual eCRF.

○ used to indicate a study procedure that did not require documentation in the individual eCRF.

§ if deemed necessary by the investigator.

* Parent(s)/LAR(s) were instructed to immediately report any convulsion (seizure) or fever ≥ 39.0°C (102.2˚F) within two days of vaccination (i.e., day of vaccination and following day).

** These were conditions which could impact the immune response (see Section 5.3.3).

Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

Table 5 List of study procedures for unprimed subjects – two vaccine doses

Age	6 to 35 months			
Epoch	Epoch 001			
Type of contact	visit	visit	visit	phone contact
Time points	Day 0	Day 28	Day 56	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	Post-Vacc 2	
Informed consent by parent(s)/LAR(s)	●			
Check inclusion/exclusion criteria	●			
Check elimination criteria (see Section 5.3.3)		●	●	●
Check contraindications to vaccination	●	●		
Collect demographic data (including weight and height)	●			
Medical history	●			
History of influenza vaccination	●			
Physical examination (history directed)	●	O §	O §	
Pre-vaccination body temperature	●	●		
Internet randomisation	●			
Blood sampling (approximately 4 mL) for humoral immune response determination	●		●	
Vaccine administration	●	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily* (Days 0-6) and unsolicited AEs (Days 0-27)	O	O		
Return of diary cards		O	O	
Diary card transcription by investigator		●	●	
Record any concomitant medication/vaccination	●	●	●	●
Record any intercurrent medical conditions **	●	●	●	●
Recording of SAEs	● #	●	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●	●
Recording of MAEs and pIMDs	●	●	●	●
Study conclusion				●

Vacc = vaccination; pIMDs = potential Immune-Mediated Diseases; LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; SAE = Serious Adverse Event

● used to indicate a study procedure that required documentation in the individual eCRF.
○ used to indicate a study procedure that did not require documentation in the individual eCRF.
§ if deemed necessary by the investigator.
* Parent(s)/LAR(s) were instructed to immediately report any convulsion (seizure) or fever ≥ 39.0°C (102.2˚F) within two days of vaccination (i.e., day of vaccination and following day).
** These were conditions which could impact the immune response (see Section 5.3.3).
# Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

5.2.2. Intervals between study visits

The time intervals between study visits of participants are presented in Table 6.

Table 6 Intervals between study visits

Interval	Optimal length of interval [1]	Allowed interval [2]
Day 0 → Day 28	28 days	25 - 42 days
Day 28 → Day 56 *	28 days	25 - 42 days
Day 0 → Day 180	180 days	166 -201 days

[1] Whenever possible the investigator had to arrange study visits within this interval.
[2] Subjects were not eligible for inclusion in the ATP cohort for analysis of immunogenicity if they had the study visit outside this interval.
*Only applicable for unprimed subjects.

5.3. Selection of study population

This study was conducted at multiple sites in three countries (Canada, Dominican Republic and Honduras). Enrolment was terminated when approximately 600 subjects were randomised and dosed.

5.3.1. Inclusion criteria for enrolment

All subjects had to satisfy ALL the following criteria at study entry:

- Subject's parent(s)/LAR(s) who, in the opinion of the investigator, could and would comply with the requirements of the protocol (e.g., completion of the diary cards, return for follow-up visits).
- A male or female between, and including, 6 and 35 months of age at the time of the first vaccination.
- Written informed consent obtained from the parent(s)/LAR(s) of the subject.
- Subjects in stable health as determined by investigator's clinical examination and assessment of subject's medical history.
- Subjects were eligible regardless of history of administration of influenza vaccine in a previous season.

5.3.2. Exclusion criteria

The following criteria were to be checked at the time of study entry. If ANY exclusion criterion applied, the subject was not included in the study:

- Use of any investigational or non-registered product (drug or vaccine) other than the study vaccine within 30 days preceding the first dose of study vaccine, or planned use during the study period. Routine registered childhood vaccinations were permitted.
- Child in care

  Please refer to the GLOSSARY OF TERMS for the definition of child in care.
- Prior receipt of any seasonal or pandemic influenza vaccine (registered or investigational) within six months preceding the first dose of study vaccine, or planned use during the study period.

- Chronic administration (defined as more than 14 days in total) of immunosuppressants or other immune-modifying drugs within six months prior to the first vaccine dose. For corticosteroids, this meant prednisone ≥ 0.5 mg/kg/day, or equivalent. Inhaled and topical steroids were allowed.
- Administration of immunoglobulins and/or any blood products within the three months preceding the first dose of study vaccine or planned administration during the study period.
- History of Guillain-Barré syndrome within 6 weeks of receipt of prior influenza vaccine.
- Any known or suspected allergy to any constituent of influenza vaccines (including egg proteins); a history of anaphylactic-type reaction to consumption of eggs; or a history of severe adverse reaction to a previous influenza vaccine.
- Acute disease and/or fever at the time of enrolment.
  - Fever was defined as temperature ≥ 38.0°C/100.4°F by any method.
  - Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever could be enrolled at the discretion of the investigator.
- Any significant disorder of coagulation or treatment with warfarin derivatives or heparin.
- Any confirmed or suspected immunosuppressive or immunodeficient condition, based on medical history and physical examination (no laboratory testing required).
- Any other condition which, in the opinion of the investigator, prevented the subject from participating in the study.

5.3.3. Elimination criteria

The use of the following concomitant medications/products/vaccines did not require withdrawal of the subject from the study but could determine a subject's evaluability in the according-to-protocol (ATP) analysis. See Section 5.10.4 for study cohorts/data sets analysed.

- Any investigational or non-registered product (drug or vaccine) other than the study vaccine(s) used during the study period.
- Immunosuppressants or other immune-modifying drugs administered chronically (i.e., more than 14 days) during the study period. For corticosteroids, this meant prednisone ≥ 0.5 mg/kg/day, or equivalent. Inhaled and topical steroids were allowed.
- Administration of influenza vaccines other than the study vaccines during the study period.
- Immunoglobulins and/or any blood products administered during the study period.

At each study visit subsequent to the first vaccination visit, it had to be verified if the subject experienced or was experiencing any intercurrent medical condition. If it was the case, the condition(s) had to be recorded in the eCRF.

Subjects could be eliminated from the ATP cohort for immunogenicity if, during the study, they incurred a condition that had the capability of altering their immune response, i.e., any confirmed or suspected immunosuppressive or immunodeficient condition, based on medical history and physical examination (no laboratory testing required).

5.3.4. Subject completion and withdrawal

5.3.4.1. Subject completion

A subject who returned for the concluding visit/was available for the concluding contact foreseen in the protocol was considered to have completed the study.

5.3.4.2. Subject withdrawal

Subjects who were withdrawn because of SAEs/AEs had to be clearly distinguished from subjects who were withdrawn for other reasons. Investigators followed subjects who were withdrawn as result of an SAE/AE until resolution of the event.

Withdrawals were not replaced.

5.3.4.2.1. Subject withdrawal from the study

From an analysis perspective, a 'withdrawal' from the study referred to any subject who did not come back for the concluding visit/was not available for the concluding contact foreseen in the protocol.

All data collected until the date of withdrawal/last contact of the subject were used for the analysis.

A subject was considered a 'withdrawal' from the study when no study procedure had occurred, no follow-up had been performed and no further information had been collected for this subject from the date of withdrawal/last contact.

Investigators made an attempt to contact those subjects who did not return for scheduled visits or follow-up.

Information relative to the withdrawal was documented in the eCRF. The investigator documented whether the decision to withdraw a subject from the study was made by the subject's parent(s) or LAR(s), or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- SAE
- Non-serious AE
- Protocol violation (specify)
- Consent withdrawal, not due to an AE*
- Moved from the study area
- Lost to follow-up
- Other (specify)

*In case a subject was withdrawn from the study because the subject's parent(s)/LAR(s) had withdrawn consent, the investigator documented the reason for withdrawal of consent, if specified by the subject, in the eCRF.

Subjects who were withdrawn from the study because of SAEs/AEs had to be clearly distinguished from subjects who were withdrawn for other reasons. Investigators followed subjects who were withdrawn from the study as result of an SAE/AE until resolution of the event.

5.3.4.2.2. Subject withdrawal from investigational vaccine/product

A 'withdrawal' from the investigational vaccine referred to any subject who did not receive the complete treatment, i.e., when no further planned dose was administered from the date of withdrawal. A subject withdrawn from the investigational vaccine could not necessarily be withdrawn from the study as further study procedures or follow-up could be performed (safety or immunogenicity) if planned in the study protocol.

Information relative to premature discontinuation of the investigational vaccine was documented on the Vaccine Administration screen of the eCRF. The investigator documented whether the decision to discontinue further vaccination/treatment was made by the subject's parent(s)/LAR(s), or by the investigator, as well as which of the following possible reasons were responsible for withdrawal:

- SAE
- Non-serious AE
- Other (specify)

5.4. Composition and administration of vaccines

5.4.1. Description of vaccines

The control vaccine (*Fluarix*) and the candidate vaccine (FLU Q-QIV) were developed and manufactured by GSK Biologicals and had a thimerosal-free formulation.

Fluarix

The TIV *Fluarix* vaccine contained HA from three influenza strains, with a total HA content of 45 µg, recommended for the influenza season 2012-2013 by the WHO, CDC/CBER, and European Medicines Agency (EMEA)/Committee for Medicinal Products for Human Use (CHMP):

- H1N1 strain: A/California/7/2009 (H1N1) (15 µg)
- H3N2 strain: A/Victoria/361/2011 (H3N2) (15 µg)
- B strain (Yamagata lineage): B/Hubei-Wujiagang/158/09 (15 µg)

The excipients used in the *Fluarix* formulations complied with the United States and/or European Pharmacopoeia (see Table 7).

Commercial vaccines were assumed to comply with the specifications given in the manufacturer's Summary of Product Characteristics (SPC).

FLU Q-QIV

The FLU Q-QIV vaccine used in the study had a total HA content of 60 µg.

It contained the same influenza A-like and B strains as those described for *Fluarix* above, as well as the most recently WHO, CDC/CBER, and EMEA/CHMP recommended B strain from the lineage not included in the 2012-2013 WHO recommendations, i.e., B/Brisbane/60/2008 like virus (15 µg):

- H1N1 strain: A/California/7/2009 (H1N1) (15 µg)
- H3N2 strain: A/Victoria/361/2011 (H3N2) (15 µg)
- B strain (Victoria lineage): B/Brisbane/60/2008 (15 µg)
- B strain (Yamagata lineage): B/Hubei-Wujiagang/158/09 (15 µg)

The excipients used in the FLU Q-QIV formulation complied with the United States and/or European Pharmacopoeia (see Table 7).

The Quality Control Standards and Requirements for the candidate vaccine were described in separate Quality Assurance documents (e.g., release protocols, certificate of analysis) and the required approvals had been obtained.

The tip caps of the prefilled syringes could contain natural rubber latex which could cause allergic reactions in latex sensitive individuals; therefore latex had to be considered a component of the vaccines.

The vaccines were labelled and packed according to applicable regulatory requirements.

Table 7 Study vaccines

Treatment name	Vaccine name	Formulation	Presentation	Volume	Number of doses	Lot numbers
Q-QIV	FLU Q-QIV	Sodium chloride, potassium chloride, sodium phosphate dibasic heptahydrate, potassium phosphate monobasic, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80) and water for injection	Translucent to off-white/greyish opalescent suspensions that could sediment slightly, presented in prefilled syringes	0.5 mL	1 (primed subjects) 2 (unprimed subjects)	DFLHA760A
D-TIV-YB	*Fluarix*	Sodium chloride, disodium phosphate dodecahydrate, potassium dihydrogen phosphate, potassium chloride, magnesium chloride hexahydrate, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), octoxynol 10 (Triton X-100), and water for injection.	Translucent to off-white/greyish opalescent suspensions that could sediment slightly, presented in prefilled syringes	0.5 mL	1 (primed subjects) 2 (unprimed subjects)	AFLUA726A

5.4.2. Dosage and administration of study vaccines

Primed subjects received a single 0.5 mL dose administered IM on Day 0. Unprimed subjects received two 0.5 mL doses administered IM on Day 0 and Day 28.

The buttock was not used for administration of vaccines because of the potential risk of injury to the sciatic nerve and the risk of decreased immunogenicity due to inadvertent subcutaneous injection or injection into deep fat tissue.

The needle for any IM injection had to be long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underlying nerves and blood vessels or bone. For injection into either the deltoid muscle or anterolateral region of the thigh, a 25 Mm (1 inch), 22-25 gauge needle was typically used. Although it was recommended to follow this guideline, an individual decision on needle size and site of injection had to be made for each person on the basis of age and muscle size. Vaccinators had to be familiar with the anatomy of the area into which they were injecting the vaccine.

The vaccine recipients were observed closely for at least 30 minutes following the administration of vaccine, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.

The vaccines were administered as indicated in Table 8 (subjects < 12 months of age) and Table 9 (subjects ≥ 12 months of age).

Table 8 Dosage and administration for subjects below 12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route [1]	Site [2]	Side
Visit Day 0	0.5 mL	Q-QIV PRIM	Q-QIV	IM	Anterolateral thigh	Left
		Q-QIV UNPRIM				
Visit Day 28	0.5 mL	Q-QIV UNPRIM				
Visit Day 0	0.5 mL	D-TIV-YB PRIM	D-TIV-YB	IM	Anterolateral thigh	Left
		D-TIV-YB UNPRIM				
Visit Day 28	0.5 mL	D-TIV-YB UNPRIM				

[1]Intramuscular (IM)
[2]Thigh injection was the recommended route for subjects < 12 months of age, however the other route (deltoid) could be considered based on the individual anatomy.

Table 9 Dosage and administration for subjects greater than or equal to 12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route [1]	Site [2]	Side
Visit Day 0	0.5 mL	Q-QIV PRIM	Q-QIV	IM	Deltoid	Non-dominant
		Q-QIV UNPRIM				
Visit Day 28	0.5 mL	Q-QIV UNPRIM				
Visit Day 0	0.5 mL	D-TIV-YB PRIM	D-TIV-YB	IM	Deltoid	Non-dominant
		D-TIV-YB UNPRIM				
Visit Day 28	0.5 mL	D-TIV-YB UNPRIM				

[1]Intramuscular (IM)
[2]Deltoid injection was the recommended route for subjects ≥ 12 months of age, however the other route (thigh) could be considered based on the individual anatomy.

5.4.3. Contraindications to subsequent vaccination

The following events constituted absolute contraindications to further administration of the FLU Q-QIV vaccine. If any of these events occurred during the study, the subject should not have received additional doses of vaccine but could continue other study procedures at the discretion of the investigator.

- Anaphylaxis following the administration of vaccine(s).

The following events constituted contraindications to administration of the study vaccines at that point in time; if any of these events occurred at the time scheduled for vaccination, the subject could be vaccinated at a later date, within the time window specified in the protocol (see Section 5.2.2), or the subject could be withdrawn at the discretion of the investigator.

- Acute disease and/or fever at the time of vaccination.
  - Fever was defined as temperature ≥ 38.0°C/100.4°F by any method.
  - Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever could be administered all vaccines.

5.4.4. Warnings and precautions

Refer to the approved product label/package insert for *Fluarix*.

5.4.5. Treatment allocation and randomisation

5.4.5.1. Randomisation of supplies

The randomisation of supplies within blocks was performed at GSK Biologicals, using MATerial EXcellence (MATEX), a program developed for use in Statistical Analysis System (SAS®) (Cary, NC, USA) by GSK Biologicals. Entire blocks were shipped to the study centres/warehouse(s).

To allow GSK Biologicals to take advantage of greater rates of recruitment than anticipated at individual centres in this multi-centre study and to thus reduce the overall study recruitment period, an over-randomisation of supplies was prepared.

5.4.5.2. Treatment allocation to the subject

The treatment numbers were allocated by dose. Each dose had a single unique treatment number throughout the study.

5.4.5.2.1. Study group and treatment number allocation

The target was to enrol approximately 600 eligible subjects who were randomly assigned to two study groups in a 1:1 ratio (approximately 300 subjects in each group).

The enrolment was performed to ensure equal distribution of the population across the two study groups, i.e., the two study groups had similar demographic characteristics (priming status, age and centre). To achieve this, allocation of the subject to a study group at the investigator site was performed using randomisation system on internet (SBIR). Within each priming status (primed or unprimed), the randomisation algorithm used a minimisation procedure accounting for age (6 to 17 months old and 18 to 35 months old) and centre. Minimisation factors had equal weight in the minimisation algorithm.

After obtaining the signed and dated informed consent form (ICF) from the subject's parent(s)/LAR(s) and having checked the eligibility of the subject, the study staff in charge of the vaccine administration accessed SBIR. Upon providing the priming status, age and the subject identification number, the randomisation system determined the study group and provided the treatment number to be used for each dose.

The number of each administered treatment had to be recorded in the eCRF on the Vaccine Administration screen.

When SBIR was not available, a reference to the SBIR user guide or the Study Procedures Manual (SPM) was made for specific instructions.

Note that as soon as the total target number of 600 subjects had been reached, the enrolment was to be frozen.

5.4.5.2.2. Treatment number allocation for subsequent doses

For each dose subsequent to the first dose, the study staff in charge of the vaccine administration accessed SBIR, provided the subject identification number, and the system provided a treatment number consistent with the allocated study group.

The number of each administered treatment had to be recorded in the eCRF on the Vaccine Administration screen.

5.5. Blinding

Data were collected in a double-blind manner.

The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

GSK Biologicals' policy (which incorporates International Conference on Harmonisation [ICH] E2A guidance, EU Clinical Trial Directive and US Federal Regulations) was to unblind the report of any SAE which was unexpected and attributable/suspected to be attributable to the investigational vaccine/product, prior to regulatory reporting. The GSK Biologicals' Central Safety Physician was responsible for unblinding the treatment assignment in accordance with the specified timeframes for expedited reporting of SAEs.

Unblinding of a subject's individual treatment code had to occur only in the case of a medical emergency, or in the event of a serious medical condition, when knowledge of the study treatment was essential for the clinical management or welfare of the subject, as judged by the investigator.

The emergency unblinding process consisted of the automated system SBIR that allowed the investigator to have unrestricted, immediate and direct access to the subject's individual study treatment.

The investigator had the option of contacting a GSK Biologicals' On-call Central Safety Physician (or backup) if he/she needed medical advice or needed the support of GSK to perform the unblinding (i.e., he/she could not access SBIR).

Any emergency unblinding had to be fully documented by using the Emergency Unblinding Documentation Form, which had to be appropriately completed by the investigator and sent within 24 hours to GSK Biologicals.

5.6. Prior and concomitant medication/vaccinations

At each study visit/contact, the investigator was to question the subject's parent(s)/LAR(s) about any medication/product taken and vaccination received by the subject.

The following concomitant medications/products/vaccines were to be recorded in the eCRF if administered during the indicated recording period:

- All concomitant medications/products, except vitamins and dietary supplements administered 30 days following each dose of study vaccine.

- Any concomitant vaccination administered in the period starting 30 days before the first dose of study vaccine and ending at the last study contact.
- Prophylactic medication (i.e., medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination).

  E.g., an antipyretic was considered to be prophylactic when it was given in the absence of fever and any other symptom, to prevent fever from occurring [fever was defined as temperature ≥ 38.0°C/100.4°F by any method].
- Any antipyretic administered in the period starting 6 hours before vaccination and ending 12 hours after vaccination.
- Any concomitant medications/products/vaccines listed in Section 5.3.3.
- Any concomitant medication/product/vaccine relevant to an SAE* or administered at any time during the study period for the treatment of an SAE*.

  * SAEs that were required to be reported per protocol.

5.7. Laboratory assays and time-points

Serological assays for the determination of antibodies against influenza virus components were performed at a GSK Biologicals' laboratory or in a laboratory designated by GSK Biologicals using standardised and validated procedures (Table 10).

Table 10 Humoral Immunity (Antibody determination)

System	Component	Method	Kit/Manufacturer	Unit	Cut-off	Laboratory
Serum	Influenza Virus A/California/7/2009 (H1N1).Hemagglutinin Ab	HI	NA	1/DIL	10	GSK Biologicals*
Serum	Influenza Virus A/Victoria/361/2011 (H3N2).Hemagglutinin Ab	HI	NA	1/DIL	10	GSK Biologicals*
Serum	Influenza Virus B/Hubei-Wujiagang/158/2009 (Yamagata).Hemagglutinin Ab**	HI	NA	1/DIL	10	GSK Biologicals*
Serum	Human influenza B/Brisbane/60/2008 (Victoria).Hemagglutinin Ab	HI	NA	1/DIL	10	GSK Biologicals*

HI = haemagglutination inhibition; NA = not applicable; 1/DIL = 1/dilution
* GSK Biologicals laboratory refers to the Global Vaccines Clinical Laboratories (GVCL) in Rixensart, Belgium; Wavre, Belgium; Laval, Canada; Dresden, Germany (only the Dresden lab was used for determination of antibodies in this study).
** The strain described was a B/Wisconsin/1/2010 like virus

The GSK Biologicals' clinical laboratories had established a Quality System supported by procedures. The activities of GSK Biologicals' clinical laboratories were audited regularly for quality assessment by an internal (sponsor-dependent) but laboratory-independent Quality Department.

5.8. Assessment of immunogenicity variables

Immunological read-outs are presented in Table 11.

Table 11 Immunological read-outs

Blood sampling time point		Sub-cohort Name	No. subjects	Component
Type of contact and time point	Sampling time point			
Visit Day 0	Pre-Vacc	All subjects	600	4 strains*
Visit Day 28	Post-Vacc 1	Primed subjects	Max 600	4 strains*
Visit Day 56	Post-Vacc 2	Unprimed subjects	Max 600	4 strains*

* Strains are described in detail in Table 10 and Section 5.4

5.8.1. Immunological correlates of protection

Although no generally accepted immunological correlate of protection has been demonstrated so far against influenza with respect to specific levels of HA-specific antibody titre post-vaccination induced with inactivated influenza virus vaccines, the protective role of antibodies against HA and, to a lesser extent, neuraminidase, is well established and has been demonstrated both in experimentally infected animals and humans [Brydak, 2000]. For this reason, the induction of antibodies was used as marker of potential vaccine efficacy and the serum haemagglutination inhibition (HI) assay was used to demonstrate this humoral response. HI antibody titres of 1:40 or greater have been associated with protection from influenza illness in at least 50% of adult subjects in some human challenge studies [Hannoun, 2004; Hobson, 1972]. While the 1:40 titre was termed “seroprotection” for convenience, it is recognised that no association of this titre with protection has been formally demonstrated in children.

5.9. Assessment of safety variables

The investigator or site staff was/were responsible for the detection, documentation and reporting of events meeting the criteria and definition of an AE or SAE as provided in the protocol.

Each subject’s parent(s)/LAR(s) were instructed to contact the investigator immediately should the subject manifest any signs or symptoms they perceived as serious.

5.9.1. Adverse events

An AE was any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An AE could therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also included failure to produce expected benefits (i.e., lack of efficacy), abuse or misuse.

Examples of an AE included:

- Significant or unexpected worsening or exacerbation of the condition/indication under study.
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after investigational vaccine administration even though they could have been present prior to the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either investigational vaccine or a concurrent medication (overdose per se did not have to be reported as an AE/SAE).
- Signs, symptoms temporally associated with vaccine administration.
- Significant failure of expected pharmacological or biological action.
- Pre- or post-treatment events that occurred as a result of protocol-mandated procedures (i.e., invasive procedures, modification of subject's previous therapeutic regimen).

AEs recorded as endpoints (solicited AEs) are described in Section 5.9.1.1. All other AEs were recorded as unsolicited AEs.

Examples of an AE did NOT include:

- Medical or surgical procedures (e.g., endoscopy, appendectomy); the condition that led to the procedure was an AE/SAE.
- Situations where an untoward medical occurrence did not occur (e.g., social and/or convenience admission to a hospital, admission for routine examination).
- Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that did not worsen.
- Pre-existing conditions or signs and/or symptoms present in a subject prior to the first study vaccination. These events were recorded in the medical history section of the eCRF.

5.9.1.1. Solicited adverse events

Solicited AEs occurring during the 7-day follow-up period after vaccination were recorded. Solicited local (injection-site) and general AEs recorded are summarised in Table 12 and Table 13, respectively.

The following local (injection-site) AEs were solicited:

Table 12 Solicited local adverse events

Pain at injection site
Redness at injection site
Swelling at injection site

The following general AEs were solicited:

Table 13 Solicited general adverse events

Drowsiness
Fever
Irritability/Fussiness
Loss of appetite

Note: Temperature was to be recorded in the evening. If additional temperature measurements were performed at other times of day, the highest temperature was to be recorded in the eCRF.

5.9.1.2. Assessment of intensity

The intensity of the following solicited AEs was assessed as described in Table 18.

Table 14 Intensity scales for solicited symptoms in infants/toddlers and children less than 6 years of age

Infant/Toddler (15–24 months)/Child (< 6 years)		
Adverse Event	**Intensity grade**	**Parameter**
Pain at injection site	0	None
	1	Mild: Minor reaction to touch
	2	Moderate: Cried/protested on touch
	3	Severe: Cried when limb was moved/spontaneously painful
Redness at injection site		Recorded greatest surface diameter in mm
Swelling at injection site		Recorded greatest surface diameter in mm
Fever*		Recorded temperature in °C/°F
Irritability/Fussiness	0	Behaviour as usual
	1	Mild: Cried more than usual/no effect on normal activity
	2	Moderate: Cried more than usual/interfered with normal activity
	3	Severe: Crying that could not be comforted/prevented normal activity
Drowsiness	0	Behaviour as usual
	1	Mild: Drowsiness easily tolerated
	2	Moderate: Drowsiness that interfered with normal activity
	3	Severe: Drowsiness that prevented normal activity
Loss of appetite	0	Appetite as usual
	1	Mild: Ate less than usual/no effect on normal activity
	2	Moderate: Ate less than usual/interfered with normal activity
	3	Severe: Did not eat at all

*Fever was defined as temperature ≥ 38.0°C / 100.4°F by any method

The maximum intensity of local injection site redness/swelling was scored at GSK Biologicals as follows:

0 : ≤ 20 mm
1 : > 20 - ≤ 50 mm
2 : > 50 - ≤ 100 mm
3 : > 100 mm

The grade of fever was scored as follows:

1	:	≥ 38.0°C (100.4°F) - ≤ 38.5°C (101.3°F)
2	:	> 38.5°C (101.3°F) - ≤ 39.0°C (102.2°F)
3	:	> 39.0°C (102.2°F) - ≤ 40.0°C (104°F)
4	:	> 40.0°C (104°F)

The investigator assessed the maximum intensity that occurred over the duration of the event for all unsolicited AEs (including SAEs) recorded during the study. The assessment was based on the investigator's clinical judgement.

The intensity was to be assigned to one of the following categories:

1 (mild)	=	An AE which was easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE which was sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE which prevented normal, everyday activities. (In a young child, such an AE would, for example, prevent attendance at kindergarten/a day-care centre and would cause the parent(s)/LAR(s) to seek medical advice.)

An AE that was assessed as Grade 3 (severe) did not have to be confused with an SAE. Grade 3 was a category used for rating the intensity of an event; and both AEs and SAEs could be assessed as Grade 3. An event was defined as 'serious' when it met one of the pre-defined outcomes as described in Section 5.9.2.

5.9.1.3. Assessment of causality

The definitions for 'NO' and 'YES' had been written in such a way that all events that had been attributed a 'NO' could be pooled with events which in the primary vaccination study were determined to be 'not related' or 'unlikely to be related' to vaccination. Those events that were attributed a 'YES' could be pooled with those events that in the past were determined to have a 'suspected' or 'probable' relationship to vaccination in the primary vaccination study.

The investigator was obligated to assess the relationship between investigational vaccine and the occurrence of each AE/SAE. The investigator used clinical judgement to determine the relationship. Alternative plausible causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational vaccine were considered and investigated. The investigator also consulted the Investigator Brochure (IB) and/or PI for marketed products to determine his/her assessment.

There could be situations when an SAE had occurred and the investigator had minimal information to include in the initial report to GSK Biologicals. However, it was very important that the investigator always made an assessment of causality for every event prior to submission of the SAE report to GSK Biologicals. The investigator could change

his/her opinion of causality in light of follow-up information and update the SAE information accordingly. The causality assessment was one of the criteria used when determining regulatory reporting requirements.

In case of concomitant administration of multiple vaccines, it could not be possible to determine the causal relationship of general AEs to the individual vaccines administered. Therefore, the investigator had to assess whether the AE could be causally related to vaccination rather than to the individual vaccines.

All solicited local (injection site) AEs were considered causally related to vaccination. Causality of all other AEs had to be assessed by the investigator using the following question:

Was there a reasonable possibility that the AE could have been caused by the investigational vaccine/product?

YES **:** There was a reasonable possibility that the vaccine(s) contributed to the AE.

NO **:** There was no reasonable possibility that the AE was causally related to the administration of the study vaccine(s). There were other, more likely causes and administration of the study vaccine(s) was not suspected to have contributed to the AE.

If an event met the criteria to be determined as 'serious' (see Section 5.9.2), additional examinations/tests were performed by the investigator in order to determine ALL possible contributing factors for each SAE.

Possible contributing factors included:

- Medical history
- Other medication
- Protocol required procedure
- Other procedure not required by the protocol
- Lack of efficacy of the vaccine, if applicable
- Erroneous administration
- Other cause (specified)

5.9.1.4. Assessments of outcomes

The investigator assessed the outcome of all unsolicited AEs (including SAEs) recorded during the study as:

- Recovered/resolved
- Recovering/resolving
- Not recovered/not resolved
- Recovered with sequelae/resolved with sequelae
- Fatal (SAEs only)

5.9.1.5. Treatment of adverse events

Treatment of any AE was at the sole discretion of the investigator and according to current good medical practice. Any medication administered for the treatment of an AE had to be recorded in the subject's eCRF (refer to Section 5.6).

5.9.1.6. Medically attended visits

For each solicited and unsolicited symptom the subject experienced, the subject's parent(s)/LAR(s) were asked if the subject received medical attention defined as hospitalisation, or an otherwise unscheduled visit to or from medical personnel for any reason, including emergency room visits. This information was recorded in the eCRF.

5.9.1.7. Potential immune-mediated diseases

PIMDs are a subset of AEs that included autoimmune diseases and other inflammatory and/or neurologic disorders of interest which could or could not have an autoimmune aetiology. AEs that needed to be recorded and reported as pIMDs included those listed in Table 15.

However, the investigator exercised his/her medical and scientific judgement in deciding whether other diseases had an autoimmune origin (i.e., pathophysiology involving systemic or organ-specific pathogenic autoantibodies) and also had to be recorded as a pIMD.

Table 15 List of potential immune-mediated diseases

Neuroinflammatory disorders	Musculoskeletal disorders	Skin disorders
• Cranial nerve disorders, including paralyses/paresis (e.g., Bell's palsy) • Optic neuritis • Multiple sclerosis • Transverse myelitis • Guillain-Barré syndrome, including Miller Fisher syndrome and other variants • Acute disseminated encephalomyelitis, including site specific variants: e.g., non-infectious encephalitis, encephalomyelitis, myelitis, myeloradiculomyelitis • Myasthenia gravis, including Lambert-Eaton myasthenic syndrome • Immune-mediated peripheral neuropathies and plexopathies, (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy). • Narcolepsy	• Systemic lupus erythematosus • Scleroderma, including diffuse systemic form and CREST syndrome • Systemic sclerosis • Dermatomyositis • Polymyositis • Antisynthetase syndrome • Rheumatoid arthritis, • Juvenile chronic arthritis, (including Still's disease) • Polymyalgia rheumatic • Spondyloarthritis, including ankylosing spondylitis, reactive arthritis (Reiter's Syndrome) and undifferentiated spondyloarthritis • Psoriatic arthropathy • Relapsing polychondritis • Mixed connective tissue disorder	• Psoriasis • Vitiligo • Erythema nodosum • Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis) • Cutaneous lupus erythematosus • Alopecia areata • Lichen planus • Sweet's syndrome • Morphoea

Liver disorders	Gastrointestinal disorders	Metabolic diseases
• Autoimmune hepatitis • Primary biliary cirrhosis • Primary sclerosing cholangitis • Autoimmune cholangitis	• Crohn's disease • Ulcerative colitis • Ulcerative proctitis • Celiac disease	• Autoimmune thyroiditis (including Hashimoto thyroiditis) • Grave's or Basedow's disease • Diabetes mellitus type I • Addison's disease

Vasculitides	Others
• Large vessels vasculitis including: giant cell arteritis such as Takayasu's arteritis and temporal arteritis. • Medium sized and/or small vessels vasculitis including: polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg–Strauss syndrome (allergic granulomatous angiitis), Buerger's disease (thromboangiitis obliterans), necrotizing vasculitis and anti-neutrophil cytoplasmic antibody (ANCA) positive vasculitis (type unspecified), Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis.	• Autoimmune hemolytic anemia • Autoimmune thrombocytopenia • Antiphospholipid syndrome • Pernicious anemia • Autoimmune glomerulonephritis (including IgA nephropathy, glomerulonephritis rapidly progressive, membranous glomerulonephritis, membranoproliferative glomerulonephritis, and mesangioproliferative glomerulonephritis) • Uveitis • Autoimmune myocarditis/cardiomyopathy • Sarcoidosis • Stevens-johnson syndrome • Sjögren's syndrome • Idiopathic pulmonary fibrosis • Goodpasture syndrome • Raynaud's phenomenon

Note: This list was based on the Medical Dictionary for Regulatory Activities (MedDRA), Version 15. The data cleaning and analysis for pIMDs had to be adjusted accordingly if the MedDRA dictionary for pIMDs was updated.

When there was enough evidence to make any of the diagnoses listed in Table 15, the AE had to be reported as a pIMD. Symptoms, signs or conditions which could (or could not) represent the diagnoses, had to be recorded and reported as AEs but not as pIMDs until the final or definitive diagnosis had been determined, and alternative diagnoses had been eliminated or shown to be less likely.

In order to facilitate the documentation of pIMDs in the eCRF, a pIMD standard questionnaire and a list of preferred terms (PTs) and PT codes corresponding to the diagnoses was available to investigators at study start.

5.9.2. Serious adverse events

An SAE was any untoward medical occurrence that:

a. Resulted in death.

b. Was life-threatening.

   Note: The term 'life-threatening' in the definition of 'serious' referred to an event in which the subject was at risk of death at the time of the event. It did not refer to an event, which hypothetically could have caused death, had it been more severe.

c. Required hospitalisation or prolongation of existing hospitalisation.

   Note: In general, hospitalisation signified that the subject had been admitted at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or in an out-patient setting. Complications that occurred during hospitalisation were also considered AEs. If a complication prolonged hospitalisation or fulfilled any other serious criteria, the event was also considered serious. When in doubt as to whether 'hospitalisation' occurred or was necessary, the AE had to be considered serious.

   Hospitalisation for elective treatment of a pre-existing condition (known or diagnosed prior to informed consent signature) that did not worsen from baseline was NOT considered an AE.

d. Resulted in disability/incapacity.

   Note: The term disability meant a substantial disruption of a person's ability to conduct normal life functions. This definition was not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhoea, influenza like illness, and accidental trauma (e.g., sprained ankle) which could interfere or prevent everyday life functions but did not constitute a substantial disruption.

Medical or scientific judgement were to be exercised in deciding whether reporting was appropriate in other situations, such as important medical events that could not be immediately life-threatening or resulted in death or hospitalisation but could jeopardise the subject or could require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These also were to be considered serious. Examples of such events were invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalisation.

5.9.2.1. Time period for detecting and recording adverse events and serious adverse events

All AEs starting within 28 days following administration of each dose of study vaccine/comparator were recorded into the appropriate section of the eCRF, irrespective of intensity or whether or not they were considered vaccination-related.

The time period for collecting and recording SAEs and pIMDs began at the first receipt of study vaccine/comparator and will end 180 days following administration of the last dose of study vaccine/comparator for each subject.

All AEs/SAEs leading to withdrawal from the study were/will be collected and recorded from the time of the first receipt of study vaccine/comparator.

SAEs that were related to the investigational vaccine were collected and recorded from the time of the first receipt of study vaccine/comparator until the subject was/will be discharged from the study.

In addition to the above-mentioned reporting requirements and in order to fulfil international reporting obligations, SAEs that were related to study participation (i.e., protocol-mandated procedures, invasive tests, a change from existing therapy) or were related to a concurrent GSK medication/vaccine were collected and recorded from the time the subject consented to participate in the study until she/he was/will be discharged from the study.

An overview of the protocol-required reporting periods for AEs and SAEs is given in Table 16.

A post-study AE/SAE was defined as any event that occurred outside of the AE/SAE reporting period defined in Table 16. The investigator was not obligated to actively seek AEs or SAEs in former study participants. However, if the investigator learned of any SAE at any time after a subject had been discharged from the study, and he/she considered the event reasonably related to the investigational vaccine/product, the investigator promptly had to notify the Study Contact for Reporting SAEs.

Table 16 Reporting periods for adverse events and serious adverse events

Event	Pre-Vacc*	Vacc 1	7 days post Vacc 1	28 days post-Vacc 1	Vacc 2**	6 days post Vacc 2**	28 days post Vacc 2**	6 months post Vacc 1
Time point		Day 0	Day 6	Day 27	Day 28	Day 34	Day 56	Day 180
Solicited local and general AEs								
Unsolicited AEs								
AEs/SAEs leading to withdrawal from the study								
SAEs related to the investigational vaccine/product								
SAEs related to study participation or concurrent GSK medication/vaccine								
SAEs, MAEs, pIMDs								
Recording of intercurrent medical conditions								

Vacc = vaccination; Pre-Vacc = pre-vaccination; (S)AE = (Serious) Adverse Event; pIMD = potential Immune-Mediate Disease; MAE = Medically Attended Adverse Event
*Informed consent obtained
**Only for unprimed subject

5.9.2.2. Evaluation of adverse events and serious adverse events

As a consistent method of collecting AEs, the subject's parent(s)/LAR(s) had to be asked a non-leading question such as:

'*Did your child act differently or feel different in any way since receiving the vaccine or since the last visit?*'

When an AE/SAE occurred, it was the responsibility of the investigator to review all documentation (e.g., hospital progress notes, laboratory and diagnostics reports) relative to the event. The investigator then recorded all relevant information regarding an AE/SAE in the eCRF. The investigator was not allowed to send photocopies of the subject's medical records to GSK Biologicals instead of appropriately completing the eCRF. However, there could be instances when copies of medical records for certain cases were requested by GSK Biologicals. In this instance, all subject identifiers were blinded on the copies of the medical records prior to submission to GSK Biologicals.

The investigator attempted to establish a diagnosis pertaining to the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis had to be documented as the AE/SAE and not the individual signs/symptoms.

5.9.2.3. Reporting of serious adverse events and other events

SAEs and pIMDs were reported promptly to GSK within the timeframes described in Table 17, once the investigator determined that the event met the protocol definition of an SAE.

Table 17 Timeframes for submitting serious adverse event and other events reports to GlaxoSmithKline (GSK) Biologicals

Type of Event	Initial Reports		Follow-up of Relevant Information on a Previous Report	
	Timeframe	Documents	Timeframe	Documents
SAEs	24 hours*	electronic SAE report	24 hours*	electronic SAE report
pIMDs	24 hours**	electronic SAE report	24 hours*	electronic SAE report

* Timeframe allowed after receipt or awareness of the information.
**Timeframe allowed after the diagnosis was established and known to the investigator.

Once an investigator became aware that an SAE had occurred in a study subject, the investigator (or designate) had to complete the information in the electronic SAE report WITHIN 24 HOURS. The SAE report was always completed as thoroughly as possible with all available details of the event. Even if the investigator did not have all information regarding an SAE, the report still had to be completed within 24 hours. Once additional relevant information was received, the report had to be updated WITHIN 24 HOURS.

The investigator always provided an assessment of causality at the time of the initial report.

If the electronic SAE reporting system did not work, the investigator (or designate) had to complete, then date and sign a paper SAE report and fax it to the GSK Biologicals Clinical Safety and Pharmacovigilance department within 24 hours.

This back-up system only had to be used if the electronic SAE reporting system was not working and NOT if the system was slow. As soon as the electronic SAE reporting system was working again, the investigator (or designate) had to complete the electronic SAE report within 24 hours. The final valid information for regulatory reporting was the information reported through the electronic SAE reporting system.

Once onset of a new pIMD or exacerbation of a pre-existing pIMD was diagnosed (serious or non-serious) in a study subject, the investigator (or designate) had to complete the information in the electronic SAE report WITHIN 24 HOURS after he/she became aware of the diagnosis. A field on the SAE report allowed to specify that the event was a pIMD and whether it was serious or non serious. The SAE report was always completed as thoroughly as possible with all available details of the event, in accordance with the pIMD standard questionnaire provided. Even if the investigator did not have all information regarding a pIMD, the report still had to be completed within 24 hours. Once additional relevant information was received, the report had to be updated WITHIN 24 HOURS.

The investigator always provided an assessment of causality at the time of the initial report.

When additional SAE or pIMD information was received after freezing of the subject's eCRF, new or updated information had to be recorded on a paper report, with all changes signed and dated by the investigator. The updated report had to be faxed to the GSK Biologicals Clinical Safety and Pharmacovigilance department or to the Study Contact for Reporting SAEs (refer to the Sponsor Information Sheet) within the designated reporting time frames specified in Table 17.

The investigator promptly reported all SAEs to GSK. GSK Biologicals had a legal responsibility to promptly notify, as appropriate, both the local regulatory authority and other regulatory agencies about the safety of a product under clinical investigation. Prompt notification of SAEs by the investigator to the Study Contact for Reporting SAEs was essential so that legal obligations and ethical responsibilities towards the safety of other subjects were met.

Investigator safety reports were prepared according to the current GSK policy and were forwarded to investigators as necessary. An investigator safety report was prepared for an SAE(s) that was both attributable to the investigational vaccine/product and unexpected. The purpose of the report was to fulfil specific regulatory and GCP requirements, regarding the product under investigation.

5.9.2.4. Follow-up of adverse events and serious adverse events

After the initial AE/SAE report, the investigator was required to proactively follow each subject and provide additional relevant information on the subject's condition to GSK Biologicals (within 24 hours for SAEs; refer to Table 17).

All SAEs and pIMDs (serious or non-serious) documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were/will be reviewed at subsequent visits/contacts until the end of the study.

With the exception of MAEs and pIMDs, all AEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were reviewed at subsequent visits/contacts until 30 days after the last vaccination.

The investigator followed subjects:

- with SAEs, pIMDs (serious or non-serious), or subjects withdrawn from the study as a result of an AE, until the event had resolved, subsided, stabilised, disappeared, or until the event was otherwise explained, or the subject was lost to follow-up.
- with MAEs or pIMDs not recovered/resolved at previous contact or visit, until the end of the study or the subjects were lost to follow-up.
- with other non-serious AEs, until Day 28 (primed subjects) or Day 56 (unprimed subjects) or they were lost to follow-up.

If the investigator received additional relevant information on a previously reported SAE, he/she provided this information to GSK Biologicals using a paper SAE report.

GSK Biologicals could request that the investigator performed or arranged the conduct of additional clinical examinations/tests and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE or SAE. The investigator was obliged to assist. If a subject died during participation in the study or during a recognised follow-up period, GSK Biologicals was provided with any available post-mortem findings, including histopathology.

5.9.3. Clinical laboratory evaluations

In absence of diagnosis, abnormal laboratory findings (e.g., clinical chemistry, haematology, urinalysis) or other abnormal assessments (e.g., physical examination findings) that were judged by the investigator to be clinically significant were recorded as AE or SAE if they met the definition of an AE or SAE (refer to Sections 5.9.1 and 5.9.2). Clinically significant abnormal laboratory findings or other abnormal assessments that were present at baseline and significantly worsened following the start of the study were also reported as AEs or SAEs. However, clinically significant abnormal laboratory findings or other abnormal assessments that were associated with the disease being studied, unless judged by the investigator as more severe than expected for the subject's condition, or that were present or detected at the start of the study and did not worsen, were not reported as AEs or SAEs.

The investigator exercised his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment was clinically significant.

5.10. Statistical methods

Statistical methods were performed as per protocol and Statistical Analysis Plan (SAP).

The statistical analyses were performed using the SAS version 9.2 on windows and StatXact-7.0 procedure on SAS.

5.10.1. Primary outcome/Efficacy Variable

- Humoral immune response to each strain of FLU Q-QIV. Serum HI antibodies on Day 0 and 28 days after the last vaccine dose were used to calculate:
  - SCRs
- Solicited local and general AEs:
  - Occurrence of solicited local and general AEs (summarised by incidence rate, duration, intensity and relationship to vaccination) during a 7-day follow-up period (i.e., day of vaccination and 6 subsequent days) after each vaccination in each group.

5.10.2. Secondary Outcome/Efficacy Variables

- Serum anti-HA antibody titres against the four vaccine strains on Day 0 and 28 days after last vaccine dose were used to calculate:
  - GMTs
  - SCRs
  - SPRs
  - MGI
- Serum anti-HA antibody titres against B/Victoria strain 28 days after last vaccine dose were used to calculate:
  - GMT ratio (FLU Q-QIV/*Fluarix*)
  - SCR difference (FLU Q-QIV – *Fluarix*)
- Unsolicited AEs
  - Occurrence of unsolicited AEs (summarised by incidence rate, intensity, and relationship to vaccination) during a 28-day follow-up period (i.e., day of vaccination and 27 subsequent days) after each vaccination, in each group.
- MAEs, SAEs, and pIMDs
  - Occurrence of MAEs, SAEs, and pIMDs (summarised by incidence rate and relationship to vaccination) during the entire study period.
- Occurrence of any fever or Grade 3 or higher fever during a 4-day follow-up period after Dose 1 or Dose 2[*].

[*]Any fever is defined as ≥ 38.0°C and Grade 3 or higher fever as ≥ 39.0°C.

5.10.3. Determination of sample size

5.10.3.1. Primary objective

The primary objective to assess the immunogenicity of SCRs in children 6 to 35 months of age who received the FLU Q-QIV vaccine was powered.

Table 18 shows the power to meet CBER immunogenicity criterion.

Table 18 Power to meet Center for Biologics Evaluation and Research (CBER) criterion in seroconversion rates (SCRs) for immunogenicity for FLU Q-QIV

Endpoint (SCR)	Reference value[1] (Seroconversion Rate)	Power[2] to reject H0: Seroconversion rate ≤ 40% N = 255 in FLU Q-QIV group
A/California/7/2009 (H1N1)	60%	>99.99%
A/Victoria/316/2011 (H3N2)	60%	>99.99%
B/Hubei-Wujiagang/158/09 (Yamagata)	60%	>99.99%
B/Brisbane/60/2008 (Victoria)	60%	>99.99%
Overall[3]		>99.99%

[1] SCRs observed in the FLU-Q-QIV 003, FLU-D-QIV 003 and *Fluarix* US-007 studies ranged from 68.1% to 92.7% (for children 6 to 35 months of age). 60% as a reference SCR was used to be conservative.
[2] Pass 2005, one-sided inequality test on proportion, alpha=2.5%; power under alternative of equal proportions of a true proportion = 0.6.
[3] Using Bonferroni adjustment on Type 2 error (beta).

Hence, with 255 evaluable subjects in the FLU Q-QIV group, an overall power of 99.99% was reached to meet CBER criterion simultaneously for all four strains. Accounting for an attrition rate of ~15%, a total of 600 subjects (300 subjects in each treatment group) was needed to be enrolled in the study.

5.10.3.2. Secondary objectives

5.10.3.2.1. Superiority of the B strain

Table 19 shows the power to demonstrate superiority of FLU Q-QIV to *Fluarix* in terms of B/Victoria antibody GMT with 255 evaluable children 6 to 35 months of age in each group.

Table 19 Power to detect superiority in haemagglutination inhibition (HI) antibody geometric mean titres (GMTs) between FLU Q-QIV and *Fluarix* for B/Victoria strain

Endpoint (GMT)	Reference value		Power[2] to reject H0: GMT ratio (FLU Q-QIV/*Fluarix*) ≤ 1.5
	Standard Deviation of log_{10} transformed titre[1]	GMT ratio (FLU Q-QIV/*Fluarix*) (FLU Q-QIV-003)	N = 255 in each group
B/Brisbane/60/2008 (Victoria)	0.7	2.6	97.03%

[1] Standard deviation of log (titres) observed in the FLU-Q-QIV 003, FLU-D-QIV 003 and *Fluarix*-007 studies ranged from 0.36 to 0.70 (for children 6 to 35 months of age).

[2] Pass 2005, non-inferiority test on means, alpha = 2.5%; equivalence margin = $|\log_{10}(0.67)|$.

Table 20 shows the power to demonstrate superiority in the B/Victoria strain SCRs between FLU Q-QIV and *Fluarix* on Day 28, with 255 evaluable children 6 to 35 months of age in each group.

Table 20 Power to detect superiority in seroconversion rates (SCRs) between FLU Q-QIV and *Fluarix* for B/Victoria strain

Endpoint (SCR)	Number of evaluable subjects in each group	SCR[1]	SCR[1]	Power[2] to reject H0: difference in SC rates (FLU Q-QIV/*Fluarix*) ≤ 10%
B/Brisbane/60/2008 (Victoria)	255	30.8%	84.3%	> 99.99%

[1] References from study FLU Q-QIV-003 (SCR from *Fluarix* = 30.8%, SCR from subjects of 6 to 35 months of age for B/Victoria strain = 84.3%).

[2] Power estimated using PASS, One-Sided exact test on the difference of proportions, H0: $\Delta \leq 0.1$, alpha = 2.5%.

The superiority of the B strain was concluded if the above both null hypotheses were rejected.

Table 21 presents the probability of observing at least one subject with any fever/Grade 3 or higher fever among all the vaccinated subjects in the FLU Q-QIV group.

Table 21 The probability to observe fever (any/Grade 3 or higher) cases in the FLU Q-QIV group

Endpoint	Observed at least	# of subjects in FLU Q-QIV	Assumed incidence rate	Probability
Any fever (≥ 38C)	1	300	5%	> 99%
Grade 3 or higher fever (≥ 39C)	1	300	1%	95.09%

5.10.4. Study cohorts /data sets analysed

5.10.4.1. Total Vaccinated cohort

The Total Vaccinated cohort (TVC) included all vaccinated subjects for whom data were available. For the total analysis of safety, this included all vaccinated subjects for whom safety data were available. For the total analysis of immunogenicity, this included vaccinated subjects for whom data concerning immunogenicity endpoint measures were available.

The TVC analysis was performed per treatment actually administered.

5.10.4.2. According-to-protocol cohort for analysis of safety

The ATP cohort for analysis of safety included all vaccinated subjects

- Who received at least one dose of study vaccine/comparator according to their random assignment.
- With sufficient data to perform an analysis of safety.
- For whom administration site of study vaccine/comparator was known.
- Who had not received a vaccine not specified or forbidden in the protocol.

5.10.4.3. According-to-protocol cohort for analysis of immunogenicity

The ATP cohort for analysis of immunogenicity, in terms of antibody response measured by the HI assay, included all evaluable subjects (i.e., those meeting all eligibility criteria, complying with the procedures and intervals defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity endpoint measures were available. Therefore, this included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination and

- Who complied with their vaccine schedule (had received one dose for primed subjects; and had received two doses for unprimed subjects).
- Who complied with the procedures and intervals defined in the protocol (refer to Table 6).
- Who did not meet any of the criteria for elimination from an ATP analysis (refer to Section 5.3.3).
- Who did not receive a product leading to elimination from an ATP analysis (refer to Section 5.3.3).
- Who did not present with a medical condition leading to elimination from an ATP analysis (refer to Section 5.3.3).

The intervals between visits/contacts were to be strictly followed. These intervals determined each subject's eligibility to be included in the ATP analyses.

5.10.5. Derived and transformed data

- **Immunogenicity**
  - The cut-off value was defined by the laboratory before the analysis and is described in Section 5.7.
  - A seronegative subject was a subject whose titre was below the cut-off value. A seropositive subject was a subject whose titre was greater than or equal to the cut-off value. For this study, HI titres of < 1:10 were considered below the cut-off.
  - The GMT calculations were performed by taking the anti-log of the mean of the log (base 10) transformed inverse titres (the number X would denote the inverse of a titre expressed as "1:X"). Antibody titres below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation.
  - The SCR was defined as the incidence rate of vaccinees who had either a pre-vaccination (Day 0) titre recorded as < 1:10 for HI and a post-vaccination titre ≥ 1:40 or a pre-vaccination titre ≥ 1:10 and at least a 4-fold increase in post-vaccination reciprocal titre.
  - The SPR was defined as the percentage of subjects who had a serum anti-HI antibody titre ≥ 1:40.
  - The MGI was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre. MGIs were calculated on Day 28 following the complete vaccination regimen.
  - The exact 95% CIs for a proportion within a group were calculated from Proc StatXact (Clopper, 1934).
  - Proc StatXact 7.0 was used to derive the standardised asymptotic 95% CI for the group difference in proportion (Newcombe, 1998); the standardised asymptotic method used within GSK Biologicals was Method 6.
  - The 95% CI for GMTs were obtained within each group separately. The 95% CI for the mean of log-transformed titre was first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs were then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titre.
  - The group GMT ratio was obtained using an Analysis of Covariance (ANCOVA) model on the logarithm-transformed titres. The ANCOVA model included the vaccine group as fixed effect and the pre-vaccination log-10 titre and age as regressors. The GMT ratio and its 95% CI were derived as exponential-transformation of the corresponding group contrast in the model.
  - Handling of missing data: for a given subject and a given immunogenicity measurement, missing or non-evaluable measurements were not replaced. Therefore, analyses excluded subjects with missing or non-evaluable measurements.

- **Reactogenicity and Safety**
  - Incidence rates of AEs were calculated as the number of subjects who experienced the event, divided by the number of subjects in the safety analysis cohort (TVC).
  - For the analysis of unsolicited AEs/MAEs/SAEs/concomitant medications, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.
  - For summaries reporting both solicited and unsolicited AEs, all vaccinated subjects were considered. Subjects who did not report the event were considered as subjects without the event.
  - Relative risk of subjects with any fever or Grade 3 or higher fever within 48 hours, 4 days post-vaccination and 7 days post-vaccination was calculated between groups with the 95% CI derived using exact method for all subjects and by age stratum.
  - Handling of missing data: For a given subject and the analysis of solicited AEs within 7 days post-vaccination (Days 0 through 6), missing or non-evaluable measurements were not replaced. Therefore, the analysis of the solicited AEs based on the TVC included only vaccinated subjects and doses with documented safety data (i.e., symptom screen/sheet completed). For analysis of unsolicited AEs, such as SAEs or AEs by primary Medical Dictionary for Regulatory Activities (MedDRA) term, all vaccinated subjects were considered. Subjects who did not report the event were considered as subjects without the event.

5.10.6. Analysis of demographics

Demographic characteristics (age, height, weight, BMI, gender, and race) of each study group were tabulated. No formal statistical evaluation of study group differences in demographic characteristics was performed.

Summary statistics for subjects' age classified by gender of the vaccinated subjects, as a whole, and per study group, were calculated.

The distribution of subjects enrolled among the study sites was tabulated as a whole and per study group, and classified subjects into disposition categories, including subjects who entered, completed, or withdrew from the study. In addition, the number of subjects in each analysis population was presented. The number of subjects who received vaccine was tabulated.

The proportion of subjects with prior immunologic experience with influenza vaccine(s) in the previous three influenza seasons were tabulated for each treatment group and categorised by priming status (primed and unprimed subjects) and age strata (6 to 17 and 18 to 35 months of age).

5.10.7. Analysis of immunogenicity

The primary analysis was based on the ATP cohort for analysis of immunogenicity. Should the percentage of vaccinated subjects with serological results excluded from the ATP cohort for analysis of immunogenicity be 5% or more, a second analysis based on the TVC had to be performed to complement the ATP analysis.

5.10.7.1. Within-groups assessment

For the humoral response in terms of HI antibodies for all vaccine strains, the following parameters (with 95% CI) were calculated by group for all subjects, each age strata (6 to 17 and 18 to 35 months of age) and by priming status (primed and unprimed):

- SCR, 28 days following last vaccination
- GMT of HI on Day 0, and 28 days following last vaccination
- MGI, 28 days following last vaccination
- SPR on Day 0, and 28 days following last vaccination

5.10.7.2. Between-groups assessment

Ratio of GMTs:

For each strain, an ANCOVA model including vaccine group as fixed effect and the $\log_{10}$ transformed pre-vaccination HI titre, age and priming status as covariates were fitted on $\log_{10}$ transformed post-vaccination HI titre.

For the B/Brisbane/60/2008 like virus (Victoria) strain:

The GMT ratio of FLU Q-QIV over *Fluarix* and the two-sided 95% CI were calculated to assess superiority.

The following evaluation criterion was considered:

- *Superiority*: the LL of two-sided 95% CI of the GMT ratio (FLU Q-QIV /*Fluarix*) had to be > 1.5.

In addition, a difference of SCR (FLU Q-QIV minus *Fluarix*) and the 95% CI was calculated to assess superiority.

The following evaluation criterion was considered:

- *Superiority: the LL of two-sided 95% CI on the SCR difference (FLU Q-QIV minus Fluarix) had to be > 10%.*

5.10.8. Analysis of safety

The primary analysis was performed on the TVC. Should the percentage of subjects excluded from the TVC be greater than 5%, a second analysis was to be performed on the ATP cohort for safety to complement the analysis of the TVC.

5.10.8.1. Within-groups assessment

- The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE during the solicited follow-up period was tabulated with exact 95% CI after each vaccine dose and overall. The percentage of doses followed by at least one local AE (solicited and unsolicited), by at least one general AE (solicited and unsolicited) and by any AE was tabulated, overall vaccination course, with exact 95% CI. The same calculations were performed for symptoms rated as Grade 3, related AEs and Grade 3 related AEs.
- The percentage of subjects reporting each individual solicited local (any, Grade 3, and medically attended) and general (any, Grade 3, related, Grade 3 related, and medically attended) AE during the 7-day solicited follow-up period was tabulated with exact 95% CI. The percentage of doses followed by each individual solicited local and general AE was tabulated, overall vaccination course, with exact 95% CI.
- The verbatim reports of unsolicited AEs were reviewed by a physician and the signs and symptoms were coded according to the MedDRA Dictionary for Adverse Reaction Terminology. The percentage of subjects with at least one report of AEs classified by MedDRA and reported up to 27 days after vaccination was tabulated with exact 95% CI. The same tabulation was performed for Grade 3 unsolicited AEs, for unsolicited AEs with a relationship to vaccination and Grade 3 unsolicited AEs with relationship to vaccination.
- MAEs, SAEs and pIMDs were/will be collected and summarised until Day 56 and through the entire follow-up period. In addition, SAEs and withdrawal due to AEs were/will be described in detail.
- The percentage of subjects reporting AEs resulting in a medically attended visit was also tabulated.

5.10.8.2. Between-groups assessment (Exploratory Analysis)

Relative risk of subjects with any fever and Grade 3 or higher fever within 4 days of the vaccination(s) was calculated for all subjects and by age stratum, along with the 95% CI.

As an exploratory analysis, relative risk of subjects with any or Grade 3 solicited AE during 7 days follow-up after vaccination(s) was calculated for all subjects and by age stratum, along with the 95% CI. Relative risk of subjects with any fever and Grade 3 or higher fever within 7 days or 48 hours of the vaccination(s) was calculated for all subjects and by age stratum, along with the 95% CI.

However, these results (relative risks) have to be interpreted with caution as alpha was not controlled (i.e., no adjustments for multiplicity).

5.10.9. Subgroup Analysis

Demographic characteristics, all immunogenicity analyses and all reactogenicity tables were tabulated for the following subgroups.

- Age (6 to 17 and 18 to 35 months of age)
- Priming status

5.10.10. Sequence of analyses

Two final analyses will be performed.

The first analysis includes safety and immunogenicity data as clean as possible up to Day 56 and is presented in this CSR.

The second analysis will be performed following the 6-month safety follow-up completion and an annex report will be generated. This analysis will be performed on clean data.

Until the last analysis has been released, access to individual treatment codes will be restricted to the statistician in charge of the analyses and authorised staff.

5.10.11. Interim analysis

There was/will be no interim analysis. All analyses were/will be conducted on final data and therefore no statistical adjustment for multiple analyses was/will be required.

5.11. Data quality assurance at study level

To ensure that the study procedures conformed across all investigator sites, the protocol, eCRF and safety reporting were reviewed with the investigator(s) and his/her/their personnel responsible for the conduct of the study by the Company representative(s) prior to study start. A multi-investigator meeting was held prior to the study start.

Adherence to the protocol requirements and verification of data generation accuracy were achieved through monitoring visits to each investigator site. Computer checks and blinded review of subject tabulations were performed to ensure consistency of eCRF completion. All procedures were performed according to methodologies detailed in GSK Biologicals Standard Operating Procedures (SOPs).

During the course of the study, issues with regard to the conduct of the study were identified, either via site monitoring activities or were brought to GSK Biologicals' attention by other oversight mechanisms. These issues were investigated and corrective and/or preventive actions where possible were taken as described in Section 6.2.3.2.

Contract Research Organisations (CROs), Emtex, Keyrus Biopharma and Business & Decision, were employed to perform medical writing, data management and laboratory management, respectively, according to an agreed contract. The CRO responsibilities were conducted according to GSK SOPs.

Independent Audit statement:

- No study specific audits were performed for this study.

5.12. Changes in the conduct of the study or planned analyses

5.12.1. Protocol amendments

The original protocol for this study was dated 30 July 2012. There were no protocol amendments.

5.12.2. Other changes

This study was conducted according to the protocol, except for the following changes:

Demographic characteristics, all immunogenicity analyses and all reactogenicity and safety tables were tabulated for each age group (6-17 and 18-35 months of age) ánd by priming status (primed, unprimed), not for a combination of the two subgroups (as stated in the protocol inadvertently).

Demographic characteristics, all immunogenicity analyses and all reactogenicity and safety tables were additionally tabulated for the following subgroups: gender, race, and country as a subgroup analysis, but were not presented in this CSR in order to avoid a voluminous document.

After completion of the study active phase, immunogenicity testing was transferred to the GSK laboratory in Dresden, Germany, instead of to the GSK laboratory in Laval. Even though the Dresden site was not listed in the study protocol, both Dresden and Laval laboratories are validated laboratories and can be back-up of each other. Therefore this change had no impact on the testing.

6. STUDY POPULATION RESULTS

6.1. Study dates

The first volunteer was enrolled in the study on 01-November-2012 and the last study visit (Day 56) was on 21-February-2013. The data lock point (date of database freeze) occurred on 15-April-2013 for the main (Day 56) analysis.

6.2. Subject eligibility and attrition from the study

The Total enrolled cohort consisted of 607 subjects, including six subjects who were not vaccinated.

A total of 299 subjects in the Q-QIV group and 302 subjects in the D-TIV-YB group received the study vaccines as planned.

6.2.1. Number of subjects

The number of subjects enrolled in the study by centre is presented in Table 22.

6.2.2. Study completion and withdrawal from study

The reasons for withdrawal are presented in Table 24 and Table 25 (overall), Table 35 and Table 36 (by age strata) and Table 41 and Table 42 (by priming status).

6.2.3. Protocol deviations at subject level

6.2.3.1. Protocol deviations leading to elimination from ATP analyses

The deviations with elimination codes are presented in Table 23.

The deviations from specifications for age and intervals between study visits for primed and unprimed subjects are presented in Table 26 and Table 27, respectively.

6.2.3.2. Protocol deviations not leading to elimination from ATP analyses

There were seven ICH/GCP-related protocol deviations identified at the site in Honduras. ICFs were either not signed properly or some of the ICF sections were not completed by the LAR. Appropriate corrective actions have been taken to assure confidence in the integrity of the data and the protection of subject's rights, safety and well-being. Therefore these deviations are not leading to elimination from ATP analyses.

6.3. Demographic characteristics

6.3.1. Total Vaccinated cohort

The demographic characteristics are presented in Table 28 (overall), Table 37 (by age strata) and Table 43 (by priming status). Vital signs characteristics at pre-vaccination are presented in Table 30.

The number of subjects with documented age at Dose 1 by gender is presented in Table 32 (overall), Table 39 (by age strata) and Table 45 (by priming status).

The history of influenza vaccination in the previous three seasons is presented in Table 34.

6.3.2. According-to-protocol cohort for immunogenicity

The demographic characteristics are presented in Table 29 (overall), Table 38 (by age strata) and Table 44 (by priming status). Vital signs characteristics at pre-vaccination are presented in Table 31.

The number of subjects with documented age at Dose 1 by gender is presented in Table 33 (overall), Table 40 (by age strata) and Table 46 (by priming status).

6.3.3. According-to-protocol for safety

Since the percentage of subjects excluded from the TVC was less than 5%, no secondary analysis was performed on the ATP cohort for safety.

7. IMMUNOGENICITY RESULTS

7.1. Data sets analysed

The analysis of immunogenicity was performed on the ATP cohort for immunogenicity (primary analysis) and the TVC (complementary analysis) as there was 5% of subjects eliminated for the ATP cohort for immunogenicity.

7.2. According-to-protocol analysis

7.2.1. Primary immunogenicity objective

The results of the immunogenicity analysis of FLU Q-QIV based on CBER's criterion for each of the four strains in children 6 to 35 months of age, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed* subjects, respectively) indicate that the SCR criterion was met: the LLs of the two-sided 95% CI for SCR were ≥ 40%:

- 81.3% for A/California/7/2009 (H1N1)
- 66.6% for A/Victoria/361/2011 (H3N2)
- 73.7% for B/Hubei-Wujiagang/158/09 (Yamagata)
- 68.4% for B/Brisbane/60/2008 (Victoria)

The results for SCR for HI antibodies against the A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Hubei-Wujiagang/158/09 (Yamagata) and B/Brisbane/60/2008 (Victoria) strains 28 days after the last vaccine dose are detailed in Table 50.

7.2.2. Secondary immunogenicity objectives

7.2.2.1. Immunogenic superiority of FLU Q-QIV over *Fluarix*

The results indicate that the pre-defined statistical criteria required for demonstration of immunogenic superiority of FLU Q-QIV versus *Fluarix*, in children 6 to 35 months of age, with respect to the B/Brisbane/60/2008 strain present in FLU Q-QIV but absent in *Fluarix*, were met (superiority criteria: LL of the two-sided 95% CI of the adjusted GMT ratio > 1.5 *and* LL of the two-sided 95% CI of the difference in SCR > 10%).

For adjusted GMT ratios:

- The LL of the two-sided 95% CI for the GMT ratio of Q-QIV over *Fluarix* for the B/Brisbane/60/2008 strain (Victoria lineage) was 5.32, which was greater than 1.5.

For the difference in SCR:

- The LL of the two-sided 95% CI for the difference in SCR of Q-QIV minus *Fluarix* for the B/Brisbane/60/2008 (Victoria lineage) strain was 57.65%, which was greater than 10%.

The results for the adjusted GMT ratio of HI antibodies between FLU Q-QIV and *Fluarix* for the B/Brisbane/60/2008 (Victoria) strain 28 days after the last vaccine dose are detailed in Table 51.

The results for the difference in SCR of HI antibodies between FLU Q-QIV and *Fluarix* for the B/Brisbane/60/2008 (Victoria) strain 28 days after the last vaccine dose are detailed in Table 52.

7.2.2.2. Haemagglutination inhibition (HI) antibody response against A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Hubei-Wujiagang/158/09 (Yamagata) and B/Brisbane/60/2008 (Victoria) strains

7.2.2.2.1. Seroconversion rates

The results for SCR for HI antibodies against the A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Hubei-Wujiagang/158/09 (Yamagata) and B/Brisbane/60/2008 (Victoria) strains 28 days after the last vaccine dose are detailed in Table 50.

7.2.2.2.2. Seropositivity rates and geometric mean titres

The results for seropositivity rates and GMTs for HI antibodies against the A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Hubei-Wujiagang/158/09 (Yamagata) and B/Brisbane/60/2008 (Victoria) strains on Day 0 and 28 days after the last vaccine dose are detailed in Table 47.

7.2.2.2.3. Seroprotection rates

The results for SPR for HI antibodies against the A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Hubei-Wujiagang/158/09 (Yamagata) and B/Brisbane/60/2008 (Victoria) strains on Day 0 and 28 days after the last vaccine dose are detailed in Table 48.

7.2.2.2.4. Mean geometric increase

The results for MGI for HI antibodies against the A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Hubei-Wujiagang/158/09 (Yamagata) and B/Brisbane/60/2008 (Victoria) strains 28 days after the last vaccine dose are detailed in Table 49.

7.2.2.2.5. Reverse cumulative distribution curves

Reverse cumulative distribution curves for HI antibodies against the A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), B/Hubei-Wujiagang/158/09 (Yamagata) and B/Brisbane/60/2008 (Victoria) strains on Day 0 and 28 days after the last vaccination are presented in Figure 2 to Figure 5.

7.3. Total Vaccinated cohort analysis

As the percentage of vaccinated subjects with serological results excluded from the ATP cohort for analysis of immunogenicity was 5%, a second analysis based on the TVC was performed to complement the ATP analysis.

Comparable results as in the ATP cohort were observed.

The immunogenicity data obtained from the analysis of the Day 56 TVC are presented in Table 69 to Table 74, and Figure 14 to Figure 17.

7.4. Subgroup analysis

Immunogenicity results were tabulated by age strata in Table 53 to Table 60 and Figure 6 to Figure 9 (ATP cohort of immunogenicity) and in Table 75 to Table 82 and Figure 18 to Figure 21 (TVC); and by priming status in Table 61 to Table 68 and Figure 10 to Figure 13 (ATP cohort of immunogenicity) and in Table 83 to Table 90 and Figure 22 to Figure 25 (TVC).

7.5. Immunogenicity summary

- The primary immunogenicity objective was met, as the LL of the two-sided 95% CI for SCR was ≥ 40% against all four strains (range 66.6% - 81.3%), approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).
- In addition, the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of GMT and SCR) was concluded (confirmatory secondary objective), as the LL of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) (5.32) was greater than 1.5, and the LL of the two-sided 95% CI for the difference in SCR (FLU Q-QIV – *Fluarix*) (57.65%) was greater than 10%.

8. SAFETY RESULTS

8.1. Data sets analysed

The analysis of safety was performed on the TVC (primary analysis).

Information regarding the number and percentage of subjects who received study vaccine per number of doses received and compliance in returning symptom sheets are detailed in Table 91 and Table 92, respectively.

8.2. Total Vaccinated cohort analysis

8.2.1. Overall incidence of adverse events

During the 7-day post-vaccination period, at least one symptom (solicited and unsolicited) was reported for 63.5% and 67.9% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Among solicited symptoms, at least one local symptom was reported for 32.8% and 31.8% of subjects, respectively, and at least one general symptom was reported for 59.9% and 62.6% of subjects, respectively.

The overall incidence of AE results are detailed in Table 93 to Table 96.

8.2.2. Solicited local adverse events

Overall, injection site pain was the most frequently reported solicited local AE (32.6% and 30.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively). Grade 3 injection site pain was reported for 7 (2.4%) and 3 (1.0%) subjects, respectively.

Redness was reported for 6 (2.1%) and 6 (2.0%) subjects in the Q-QIV and D-TIV-YB groups, respectively, and swelling for 5 (1.7%) and 6 (2.0%) subjects, respectively. No grade 3 redness or swelling was reported.

After Dose 1, the incidence of injection site pain was 25.2% and 21.5% of subjects in the Q-QIV and D-TIV-YB groups, respectively. After Dose 2, the incidence of injection site pain was 20.8% and 21.4% of subjects, respectively.

Solicited local AE results are detailed in Table 97.

8.2.3. Solicited general adverse events

Overall, irritability/fussiness was the most frequently reported solicited general AE (40.7% and 41.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively). Grade 3 irritability/fussiness was reported for 5.2% and 4.7% of subjects, respectively.

Loss of appetite was reported for 34.1% and 33.8% of subjects in the Q-QIV and D-TIV-YB groups, respectively, and drowsiness for 32.1% and 29.7% of subjects, respectively.

Fever was reported for 21.0% and 20.3% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Grade 3 or higher fever was reported for 7.9% and 4.4% of subjects, respectively.

The incidence of solicited AEs after Dose 1 for subjects in the Q-QIV and D-TIB-YB groups, respectively, was 24.9% and 21.6% for drowsiness, 31.5% and 31.8% for irritability/fussiness, 27.0% and 24.0% for loss of appetite, and 14.5% and 14.5% for fever. After Dose 2, the incidence was respectively 18.0% and 15.9% for drowsiness, 26.5% and 27.2% for irritability/fussiness, 17.6% and 19.9% for loss of appetite, and 10.3% and 9.1% for fever.

Solicited general AE (excluding fever) results are detailed in Table 98. Results for fever are detailed in Table 99.

8.2.4. Unsolicited adverse events

During the 28-day post-vaccination period, at least one unsolicited AE was reported for 47.5% and 54.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Nasopharyngitis (26.1% and 29.8% of subjects, respectively) and diarrhoea (12.7% and 12.6% of subjects, respectively) were the only two unsolicited AEs reported for more than 5.0% of subjects.

At least one Grade 3 unsolicited AE was reported for 9 (3.0%) and 5 (1.7%) subjects in the Q-QIV and D-TIV-YB groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 5.7% and 4.3% of subjects, respectively. At least one Grade 3 unsolicited AE with causal relationship to vaccination was reported for 1 (0.3%) and no subject, respectively.

Unsolicited AEs are detailed in Table 100 to Table 111.

8.3. According-to-protocol cohort analysis

The primary analysis of safety was performed on the TVC. Since the percentage of enrolled subjects excluded from the TVC for analysis of safety was less than 5%, no secondary analysis on the ATP cohort for safety was performed.

8.4. Serious adverse events

A total of four SAEs were reported for three subjects (1 [0.3%)] and 2 [0.7%] subjects in the Q-QIV and D-TIV-YB groups, respectively) during the entire study period until Day 56. None of these SAEs was fatal or considered related to the study vaccine in the opinion of the investigator.

The SAE Summary Tables are presented in Section 13.1 and the SAE Council for International Organisations of Medical Sciences (CIOMS) reports are presented in Section 13.2.

SAE results are detailed in Table 115 to Table 117.

8.4.1. Fatal events

No subject died during this study up to Day 56.

8.4.2. Non-fatal events

A total of four non-fatal SAEs were reported for three subjects during the entire study period until Day 56. All events were considered recovered or resolved at the time of this report. None of these events was considered related to the study vaccine in the opinion of the investigator. Non-fatal SAEs are detailed in Table 206 in Section 13.1.

8.5. Medically attended adverse events

At least one unsolicited AE with a medically attended visit up to Day 56 was reported for 32.4% and 33.4% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Nasopharyngitis (17.4% and 17.9% of subjects, respectively) and diarrhoea (6.0% and 7.3% of subjects, respectively) were the only two MAEs reported by more than 5.0% of subjects.

MAE results are detailed in Table 112 to Table 114.

8.6. Adverse events leading to premature discontinuation of study vaccine and/or study

No (S)AEs leading to premature discontinuation of study vaccine were reported in this study from Day 0 to Day 56.

8.7. Other significant adverse events

One case of febrile convulsion was reported in a 18 month old unprimed male subject in the Q-QIV group 6 hours after dose 1. The case was a simple partial convulsion with eyeball rolling and mild stiffness of the upper extremities that lasted about eight seconds. The case was considered related to the study vaccine by the investigator, with no concomitant infections reported. Subject was attended at the emergency room but not hospitalized, and recoved with no sequela. Dose 2 was given as scheduled, and no fever was reported after the second dose.

8.7.1. Potential immune-mediated diseases

From Day 0 to Day 56, no pIMDs were reported.

8.8. Relative risk of solicited AEs and fever (Exploratory analysis)

Overall, there was no meaningful difference in relative risk for any (and Grade 3) solicited local and general AEs between both study groups during the 7-day post-vaccination period.

The relative risk of any fever for Q-QIV compared to D-TIV-YB during a 4-day follow-up period was 1.12 with a 95% CI of [0.76; 1.64] (p-value = 0.6439). The relative risk of Grade 3 or higher fever for Q-QIV compared to D-TIV-YB during a 4-day follow-up period was 2.04 with a 95% CI of [0.91; 4.60] (p-value = 0.0977).

The relative risk of any fever during a 4-day follow-up period after Dose 1 was 1.26 with a 95% CI of [0.77, 2.05] (p-value = 0.4071), and 1.18 with a 95% CI of [0.65, 2.16] (p-value = 0.6211) after Dose 2.

The relative risk of Grade 3 or higher fever during a 4-day follow-up period after Dose 1 was 1.54 with a 95% CI of [0.47, 5.03] (p-value = 0.5409), and 2.54 with a 95% CI of [0.85, 7.58] (p-value = 0.1115) after Dose 2.

However, these results should be interpreted with caution as the sample size was small and alpha was not controlled (i.e., no adjustments for multiplicity).

Results are detailed in Table 120 to Table 124.

8.9. Concomitant medications /vaccinations

Up to Day 56, any concomitant medications were used by 52.5% and 56.0% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Any antipyretic was taken by 31.8% and 32.8% of subjects, respectively. Antipyretics were taken prophylactically in anticipation of reaction to vaccination by 3.0% and 2.6% of subjects, respectively.

The results regarding concomitant medications are detailed in Table 125.

8.10. Important safety information received after the data lock point (database freeze date)

One report of a potential immune-mediated disorder was received after the data lock point of this report. This report described a three year-old female who developed hair loss 65 days after the second blinded dose of vaccine. The subject was evaluated in the office one week later, and found to have an area of alopecia over the anterior part of the scalp. A diagnosis of alopecia areata was made, and the hair loss slowly improved within 4 weeks time, without any treatment. This pIMD was considered to be non-serious, and the investigator did not consider the event to be related to the investigational product. This late-breaking information does not change the safety profile of the data presented in this report.

8.11. Subgroup analysis

As a subgroup analysis, reactogenicity and safety results were tabulated by age strata in Table 126 to Table 165; and by priming status in Table 166 to Table 205.

8.12. Safety summary

A descriptive summary of safety data is provided in this section. These data, together with the safety data from other studies will contribute to the safety evaluation of the product.

- During the 7-day post-vaccination period, at least one symptom (solicited and unsolicited) was reported for 63.5% and 67.9% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Among solicited symptoms, at least one local symptom was reported for 32.8% and 31.8% of subjects, respectively, and at least one general symptom was reported for 59.9% and 62.6% of subjects, respectively.
- Injection site pain was the most frequently reported solicited local AE (32.6% and 30.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively). Grade 3 injection site pain was reported for 7 (2.4%) and 3 (1.0%) subjects, respectively.
- Irritability/fussiness was the most frequently reported solicited general AE (40.7% and 41.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively). Grade 3 irritability/fussiness was reported for 5.2% and 4.7% of subjects, respectively.
- During the 28-day post-vaccination period, at least one unsolicited AE was reported for 47.5% and 54.6% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Nasopharyngitis (26.1% and 29.8% of subjects, respectively) and diarrhoea (12.7% and 12.6% of subjects, respectively) were the only two unsolicited AEs reported by more than 5.0% of subjects. Only for one subject in the Q-QIV group a Grade 3 unsolicited AE with causal relationship to vaccination was reported.
- A total of four SAEs were reported for three subjects during the entire study period until Day 56. None of these SAEs were considered related to the study vaccine in the opinion of the investigator.
- At least one unsolicited AE with a medically attended visit up to Day 56 was reported for 32.4% and 33.4% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Nasopharyngitis (17.4% and 17.9% of subjects, respectively) and diarrhoea (6.0% and 7.3% of subjects, respectively) were the only two MAEs reported by more than 5.0% of subjects.
- No subject withdrew due to an AE or SAE from Day 0 to Day 56.
- No pIMDs were reported up to Day 56.
- The relative risk of any fever for Q-QIV compared to D-TIV-YB during a 4-day follow-up period was 1.12 with a 95% CI of [0.76; 1.64] (p-value = 0.6439). The relative risk of Grade 3 or higher fever for Q-QIV compared to D-TIV-YB during a 4-day follow-up period was 2.04 with a 95% CI of [0.91; 4.60] (p-value = 0.0977).

9. OVERALL CONCLUSIONS

The following conclusions can be made based on the study results:

- The primary immunogenicity objective was met. For all four strains, the LL of the two-sided 95% CI for SCR was ≥ 40% (range 66.6% - 81.3%) approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).
- During the 7-day post-vaccination period, at least one symptom (solicited and unsolicited) was reported for 63.5% and 67.9% of subjects in the Q-QIV and D-TIV-YB groups, respectively. Injection site pain was the most frequently reported solicited local AE (32.6% and 30.6% of subjects, respectively) and irritability/fussiness the most frequently reported solicited general AE (40.7% and 41.6% of subjects, respectively).
- The secondary objective of immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of GMT and SCR) was also met. The LL of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluarix*) (5.32) was greater than 1.5 and the LL of the two-sided 95% CI for the difference in SCR (FLU Q-QIV - *Fluarix*) (57.65%) was greater than 10%.
- No other safety concerns were identified. The FLU Q-QIV and *Fluarix* vaccines were generally well tolerated.

10. TABLES AND FIGURES

10.1. Demographic characteristics

10.1.1. Overall

Table 22 Number of subjects by centre (Total Vaccinated cohort)

	Q-QIV	D-TIV-YB	Total	
Centre	**n**	**n**	**n**	**%**
105457	125	125	250	41.6
105458	105	105	210	34.9
105601	16	14	30	5.0
105602	15	17	32	5.3
105604	9	11	20	3.3
105605	9	9	18	3.0
105606	9	10	19	3.2
105607	11	11	22	3.7
All	299	302	601	100

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
n = number of subjects included in each group or in total for a given centre or for all centres
All = sum of all subjects in each group or in total (sum of all groups)
% = n/All x 100
Centre = GSK Biologicals assigned centre number

Table 23 Number of subjects enrolled in the study and number of subjects excluded from ATP analyses with reasons for exclusion

	Total			Q-QIV		D-TIV-YB		NOGRP	
Title	**n**	**s**	**%**	**n**	**s**	**n**	**s**	**n**	**s**
Total enrolled cohort	607			300		302		5	
Study vaccine dose not administrated but subject number allocated (code 1030)	6	6		1	1	0	0	5	5
Total Vaccinated cohort	601		100	299		302		0	
Randomisation failure (code 1050)	1	1		0	0	1	1	0	0
ATP cohort for safety	600		99.8	299		301		0	
Underlying medical condition forbidden by the protocol (code 2050)	1	1		1	1	0	0	0	0
Non compliance with vaccination schedule (including wrong and unknown dates) (code 2080)	6	6		2	2	4	4	0	0
Non compliance with blood sampling schedule (including wrong and unknown dates (code 2090)	1	2		0	0	1	2	0	0
Essential serological data missing (code 2100)	21	22		12	13	9	9	0	0
ATP cohort for immunogenicity	571		95.0	284		287		0	

NOGRP = No assigned group
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
Note: Subjects may have more than one elimination code assigned
n = number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
s = number of subjects with the elimination code assigned
% = percentage of subjects in the considered ATP cohort relative to the Total Vaccinated cohort

Table 24 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal (Total Vaccinated cohort)

	Q-QIV	D-TIV-YB	Total
Number of subjects vaccinated	299	302	601
Number of subjects completed	286	294	580
Number of subjects withdrawn	13	8	21
Reasons for withdrawal :			
Serious Adverse Event	0	0	0
Non-Serious Adverse Event	0	0	0
Protocol violation	0	0	0
Consent withdrawal (not due to an adverse event)	7	6	13
Migrated/moved from study area	2	1	3
Lost to follow-up (subjects with incomplete vaccination course)	3	1	4
Lost to follow-up (subjects with complete vaccination course)	1	0	1
Sponsor study termination	0	0	0
Others	0	0	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last visit

Table 25 Number of subjects at each visit and list of withdrawn subjects (Total vaccinated cohort)

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
Q-QIV	VISIT 1 DAY 0	299		
			(b) (6)	Consent withdrawal, not due to an adverse event
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Migrated / moved from the study area
				Consent withdrawal, not due to an adverse event
	VISIT 2 DAY 28	290		
				Lost to follow-up
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Migrated / moved from the study area
	VISIT 3 DAY 56	273		
D-TIV-YB	VISIT 1 DAY 0	302		
				Lost to follow-up
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
				Consent withdrawal, not due to an adverse event
	VISIT 2 DAY 28	296		

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	
				Migrated / moved from the study area
				Consent withdrawal, not due to an adverse event
	VISIT 3 DAY 56	279		

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
N = Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

Table 26 Deviations from specifications for age and intervals between study visits for primed subjects (Total Vaccinated cohort)

		Age	Dose:1-PI(D28)
Group		**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days
Q-QIV	N	13	13
	n	0	0
	%	0.0	0.0
	range	18 to 34	27 to 42
D-TIV-YB	N	15	15
	n	0	0
	%	0.0	0.0
	range	16 to 34	27 to 39
Total	N	28	28
	n	0	0
	%	0.0	0.0
	range	16 to 34	27 to 42

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Table 27 Deviations from specifications for age and intervals between study visits for unprimed subjects (Total Vaccinated cohort)

		Age	Dose:1-Dose:2	Dose:2-PII(D56)
Group		**Protocol**	**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days	from 25 to 42 days
Q-QIV	N	286	277	273
	n	0	2	0
	%	0.0	0.7	0.0
	range	6 to 35	25 to 45	25 to 42
D-TIV-YB	N	287	281	278
	n	0	4	2
	%	0.0	1.4	0.7
	range	6 to 35	25 to 63	25 to 49
Total	N	573	558	551
	n	0	6	2
	%	0.0	1.1	0.4
	range	6 to 35	25 to 63	25 to 49

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Table 28 Summary of demographic characteristics (Total Vaccinated cohort)

		Q-QIV N = 299		D-TIV-YB N = 302		Total N = 601	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	18.2	-	18.1	-	18.1	-
	SD	8.17	-	8.34	-	8.25	-
	Median	17.0	-	16.5	-	17.0	-
	Minimum	6	-	6	-	6	-
	Maximum	35	-	35	-	35	-
Gender	Female	155	51.8	146	48.3	301	50.1
	Male	144	48.2	156	51.7	300	49.9
Ethnicity	American hispanic or latino	231	77.3	233	77.2	464	77.2
	Not american hispanic or latino	68	22.7	69	22.8	137	22.8
Geographic Ancestry	African heritage / african american	4	1.3	2	0.7	6	1.0
	American indian or alaskan native	0	0.0	0	0.0	0	0.0
	Asian - central / south asian heritage	16	5.4	14	4.6	30	5.0
	Asian - east asian heritage	0	0.0	0	0.0	0	0.0
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	0	0.0	2	0.7	2	0.3
	Native hawaiian or other pacific islander	0	0.0	0	0.0	0	0.0
	White - arabic / north african heritage	1	0.3	0	0.0	1	0.2
	White - caucasian / european heritage	47	15.7	52	17.2	99	16.5
	Other	231	77.3	232	76.8	463	77.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 29 Summary of demographic characteristics (ATP cohort for immunogenicity)

		Q-QIV N = 284		D-TIV-YB N = 287		Total N = 571	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	18.1	-	18.1	-	18.1	-
	SD	8.22	-	8.33	-	8.27	-
	Median	16.0	-	17.0	-	17.0	-
	Minimum	6	-	6	-	6	-
	Maximum	35	-	35	-	35	-
Gender	Female	149	52.5	139	48.4	288	50.4
	Male	135	47.5	148	51.6	283	49.6
Ethnicity	American hispanic or latino	223	78.5	223	77.7	446	78.1
	Not american hispanic or latino	61	21.5	64	22.3	125	21.9
Geographic Ancestry	African heritage / african american	4	1.4	2	0.7	6	1.1
	American indian or alaskan native	0	0.0	0	0.0	0	0.0
	Asian - central / south asian heritage	15	5.3	13	4.5	28	4.9
	Asian - east asian heritage	0	0.0	0	0.0	0	0.0
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	0	0.0	2	0.7	2	0.4
	Native hawaiian or other pacific islander	0	0.0	0	0.0	0	0.0
	White - arabic / north african heritage	1	0.4	0	0.0	1	0.2
	White - caucasian / european heritage	41	14.4	47	16.4	88	15.4
	Other	223	78.5	223	77.7	446	78.1

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 30 Summary of vital signs characteristics at pre-vaccination (Total Vaccinated cohort)

		Q-QIV (N = 299)	D-TIV-YB (N = 302)	Total (N = 601)
Characteristics	**Parameters**	**Value**	**Value**	**Value**
Height (Cm)	Mean	80.4	80.2	80.3
	SD	8.49	8.37	8.42
	Median	80.0	80.0	80.0
	Minimum	61.0	61.0	61.0
	Maximum	106.0	107.0	107.0
	Unknown	0	0	0
Weight (Kg)	Mean	11.1	11.2	11.1
	SD	2.39	2.67	2.54
	Median	10.9	10.9	10.9
	Minimum	4.5	6.5	4.5
	Maximum	22.2	29.8	29.8
	Unknown	0	0	0
BMI (kg/m²)	Mean	17.1	17.3	17.2
	SD	1.94	2.42	2.20
	Median	17.0	17.1	17.0
	Minimum	7.2	10.6	7.2
	Maximum	23.2	39.4	39.4
	Unknown	0	0	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 31 Summary of vital signs characteristics at pre-vaccination (ATP cohort for immunogenicity)

		Q-QIV (N = 284)	D-TIV-YB (N = 287)	Total (N = 571)
Characteristics	**Parameters**	**Value**	**Value**	**Value**
Height (Cm)	Mean	80.4	80.2	80.3
	SD	8.58	8.35	8.46
	Median	80.0	80.0	80.0
	Minimum	61.0	61.0	61.0
	Maximum	106.0	107.0	107.0
	Unknown	0	0	0
Weight (Kg)	Mean	11.1	11.2	11.1
	SD	2.42	2.63	2.52
	Median	10.9	10.9	10.9
	Minimum	4.5	6.5	4.5
	Maximum	22.2	29.8	29.8
	Unknown	0	0	0
BMI (kg/m²)	Mean	17.1	17.3	17.2
	SD	1.96	2.43	2.21
	Median	17.0	17.1	17.0
	Minimum	7.2	10.6	7.2
	Maximum	23.2	39.4	39.4
	Unknown	0	0	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 32 Age (in months) at vaccination Dose 1 by gender (Total Vaccinated cohort)

Group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	F	155	155	18.1	7.82	6	35
	M	144	144	18.2	8.57	6	35
	Total	299	299	18.2	8.17	6	35
D-TIV-YB	F	146	146	18.3	8.58	6	35
	M	156	156	17.9	8.14	6	35
	Total	302	302	18.1	8.34	6	35
ALL	F	301	301	18.2	8.18	6	35
	M	300	300	18.0	8.34	6	35
	Total	601	601	18.1	8.25	6	35

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
F = female; M = male
N = number of subjects with documentation on gender
N with age= number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 33 Age (in months) at vaccination Dose 1 by gender (ATP cohort for immunogenicity)

Group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	F	149	149	18.0	7.79	6	35
	M	135	135	18.3	8.70	6	35
	Total	284	284	18.1	8.22	6	35
D-TIV-YB	F	139	139	18.1	8.46	6	35
	M	148	148	18.2	8.22	6	35
	Total	287	287	18.1	8.33	6	35
ALL	F	288	288	18.1	8.11	6	35
	M	283	283	18.2	8.44	6	35
	Total	571	571	18.1	8.27	6	35

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
F = female; M = male
N = number of subjects with documentation on gender
N with age= number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 34 History of influenza vaccination in the previous 3 seasons (Total Vaccinated cohort)

		Q-QIV N = 299		D-TIV-YB N = 302		Total N = 601	
Characteristics	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
At least one season	Yes	16	5.4	23	7.6	39	6.5
	No	283	94.6	279	92.4	562	93.5
Season 2009-2010	Yes	0	0	0	0	0	0
Season 2010-2011	Yes	4	1.3	4	1.3	8	1.3
Season 2011-2012	Yes	13	4.3	21	7.0	34	5.7

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = Total number of subjects
n = number of subjects with influenza vaccination during the specified season
% = n / Number of subjects with available results x 100

10.1.2. By age strata

Table 35 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal by age strata (Total vaccinated cohort)

	Q-QIV		D-TIV-YB		Total	
	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
Number of subjects vaccinated	157	142	160	142	317	284
Number of subjects completed	152	134	153	141	305	275
Number of subjects withdrawn	5	8	7	1	12	9
Reasons for withdrawal :						
Serious Adverse Event	0	0	0	0	0	0
Non-Serious Adverse Event	0	0	0	0	0	0
Protocol violation	0	0	0	0	0	0
Consent withdrawal (not due to an adverse event)	4	3	5	1	9	4
Migrated/moved from study area	1	1	1	0	2	1
Lost to follow-up (subjects with incomplete vaccination course)	0	3	1	0	1	3
Lost to follow-up (subjects with complete vaccination course)	0	1	0	0	0	1
Sponsor study termination	0	0	0	0	0	0
Others	0	0	0	0	0	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last visit

Table 36 Number of subjects at each visit and list of withdrawn subjects by age strata (Total vaccinated cohort)

Group	Sub-group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
Q-QIV	6-17M	VISIT 1 DAY 0	157		
				(b) (6)	Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
		VISIT 2 DAY 28	155		
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Migrated / moved from the study area
		VISIT 3 DAY 56	152		
	18-35M	VISIT 1 DAY 0	142		
					Consent withdrawal, not due to an adverse event
					Lost to follow-up
					Lost to follow-up
					Lost to follow-up
					Consent withdrawal, not due to an adverse event
					Migrated / moved from the study area
					Consent withdrawal, not due to an adverse event
		VISIT 2 DAY 28	135		
					Lost to follow-up
		VISIT 3 DAY 56	121		
D-TIV-YB	6-17M	VISIT 1 DAY 0	160		
					Lost to follow-up
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
		VISIT 2 DAY 28	155		
					Migrated / moved from the study area
					Consent withdrawal, not due to an adverse event
		VISIT 3 DAY 56	152		
	18-35M	VISIT 1 DAY 0	142		
					Consent withdrawal, not due to an adverse event
		VISIT 2 DAY 28	141		

Group	Sub-group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
				(b) (6)	
		VISIT 3 DAY 56	127		

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

Table 37 Summary of demographic characteristics (By age strata - Total Vaccinated cohort)

		Q-QIV				D-TIV-YB				Total			
		6-17M N = 157		18-35M N = 142		6-17M N = 160		18-35M N = 142		6-17M N = 317		18-35M N = 284	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	11.4	-	25.6	-	11.4	-	25.6	-	11.4	-	25.6	-
	SD	3.18	-	4.93	-	3.30	-	5.28	-	3.24	-	5.10	-
	Median	12.0	-	25.0	-	12.0	-	25.0	-	12.0	-	25.0	-
	Minimum	6	-	18	-	6	-	18	-	6	-	18	-
	Maximum	17	-	35	-	17	-	35	-	17	-	35	-
Gender	Female	83	52.9	72	50.7	73	45.6	73	51.4	156	49.2	145	51.1
	Male	74	47.1	70	49.3	87	54.4	69	48.6	161	50.8	139	48.9
Ethnicity	American hispanic or latino	123	78.3	108	76.1	127	79.4	106	74.6	250	78.9	214	75.4
	Not american hispanic or latino	34	21.7	34	23.9	33	20.6	36	25.4	67	21.1	70	24.6
Geographic Ancestry	African heritage / african american	1	0.6	3	2.1	0	0.0	2	1.4	1	0.3	5	1.8
	American indian or alaskan native	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - central / south asian heritage	10	6.4	6	4.2	7	4.4	7	4.9	17	5.4	13	4.6
	Asian - east asian heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	0	0.0	0	0.0	1	0.6	1	0.7	1	0.3	1	0.4
	Native hawaiian or other pacific islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - arabic / north african heritage	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.4
	White - caucasian / european heritage	22	14.0	25	17.6	25	15.6	27	19.0	47	14.8	52	18.3
	Other	124	79.0	107	75.4	127	79.4	105	73.9	251	79.2	212	74.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter; SD = standard deviation

Table 38 Summary of demographic characteristics (By age strata - ATP cohort for immunogenicity)

		Q-QIV				D-TIV-YB				Total			
		6-17M N = 151		18-35M N = 133		6-17M N = 149		18-35M N = 138		6-17M N = 300		18-35M N = 271	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	11.5	-	25.7	-	11.3	-	25.5	-	11.4	-	25.6	-
	SD	3.18	-	4.97	-	3.32	-	5.28	-	3.25	-	5.12	-
	Median	12.0	-	25.0	-	12.0	-	25.0	-	12.0	-	25.0	-
	Minimum	6	-	18	-	6	-	18	-	6	-	18	-
	Maximum	17	-	35	-	17	-	35	-	17	-	35	-
Gender	Female	80	53.0	69	51.9	70	47.0	69	50.0	150	50.0	138	50.9
	Male	71	47.0	64	48.1	79	53.0	69	50.0	150	50.0	133	49.1
Ethnicity	American hispanic or latino	118	78.1	105	78.9	119	79.9	104	75.4	237	79.0	209	77.1
	Not american hispanic or latino	33	21.9	28	21.1	30	20.1	34	24.6	63	21.0	62	22.9
Geographic Ancestry	African heritage / african american	1	0.7	3	2.3	0	0.0	2	1.4	1	0.3	5	1.8
	American indian or alaskan native	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - central / south asian heritage	10	6.6	5	3.8	7	4.7	6	4.3	17	5.7	11	4.1
	Asian - east asian heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	0	0.0	0	0.0	1	0.7	1	0.7	1	0.3	1	0.4
	Native hawaiian or other pacific islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - arabic / north african heritage	0	0.0	1	0.8	0	0.0	0	0.0	0	0.0	1	0.4
	White - caucasian / european heritage	21	13.9	20	15.0	21	14.1	26	18.8	42	14.0	46	17.0
	Other	119	78.8	104	78.2	120	80.5	103	74.6	239	79.7	207	76.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 39 Age (in months) at vaccination Dose 1 by gender (By age strata - Total Vaccinated cohort)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	6-17M	F	83	83	11.9	3.17	6	17
		M	74	74	11.0	3.15	6	17
		Total	157	157	11.4	3.18	6	17
	18-35M	F	72	72	25.2	4.88	18	35
		M	70	70	25.9	4.99	18	35
		Total	142	142	25.6	4.93	18	35
D-TIV-YB	6-17M	F	73	73	11.0	3.45	6	17
		M	87	87	11.6	3.15	6	17
		Total	160	160	11.4	3.30	6	17
	18-35M	F	73	73	25.5	5.51	18	35
		M	69	69	25.7	5.07	18	35
		Total	142	142	25.6	5.28	18	35
ALL	6-17M	F	156	156	11.5	3.32	6	17
		M	161	161	11.3	3.16	6	17
		Total	317	317	11.4	3.24	6	17
	18-35M	F	145	145	25.4	5.19	18	35
		M	139	139	25.8	5.01	18	35
		Total	284	284	25.6	5.10	18	35

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age= number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 40 Age (in months) at vaccination Dose 1 by gender (By age strata - ATP cohort for immunogenicity)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	6-17M	F	80	80	11.9	3.16	6	17
		M	71	71	11.0	3.16	6	17
		Total	151	151	11.5	3.18	6	17
	18-35M	F	69	69	25.1	4.95	18	35
		M	64	64	26.3	4.96	18	35
		Total	133	133	25.7	4.97	18	35
D-TIV-YB	6-17M	F	70	70	11.1	3.46	6	17
		M	79	79	11.6	3.21	6	17
		Total	149	149	11.3	3.32	6	17
	18-35M	F	69	69	25.3	5.51	18	35
		M	69	69	25.7	5.07	18	35
		Total	138	138	25.5	5.28	18	35
ALL	6-17M	F	150	150	11.5	3.32	6	17
		M	150	150	11.3	3.18	6	17
		Total	300	300	11.4	3.25	6	17
	18-35M	F	138	138	25.2	5.22	18	35
		M	133	133	26.0	5.01	18	35
		Total	271	271	25.6	5.12	18	35

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age= number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

10.1.3. By priming status

Table 41 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal by priming status (Total vaccinated cohort)

	Q-QIV		D-TIV-YB		Total	
	UNPRIMED	PRIM	UNPRIMED	PRIM	UNPRIMED	PRIM
Number of subjects vaccinated	286	13	287	15	573	28
Number of subjects completed	273	13	279	15	552	28
Number of subjects withdrawn	13	0	8	0	21	0
Reasons for withdrawal :						
Serious Adverse Event	0	0	0	0	0	0
Non-Serious Adverse Event	0	0	0	0	0	0
Protocol violation	0	0	0	0	0	0
Consent withdrawal (not due to an adverse event)	7	0	6	0	13	0
Migrated/moved from study area	2	0	1	0	3	0
Lost to follow-up (subjects with incomplete vaccination course)	3	0	1	0	4	0
Lost to follow-up (subjects with complete vaccination course)	1	0	0	0	1	0
Sponsor study termination	0	0	0	0	0	0
Others	0	0	0	0	0	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
UNPRIMED = Unprimed subjects
PRIM = Primed subjects
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last visit

Table 42 Number of subjects at each visit and list of withdrawn subjects by priming status (Total vaccinated cohort)

Group	Sub-group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
Q-QIV	UNPRIMED	VISIT 1 DAY 0	286		
				(b) (6)	Consent withdrawal, not due to an adverse event
					Lost to follow-up
					Lost to follow-up
					Lost to follow-up
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Migrated / moved from the study area
					Consent withdrawal, not due to an adverse event
		VISIT 2 DAY 28	277		
					Lost to follow-up
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Migrated / moved from the study area
		VISIT 3 DAY 56	273		
	PRIM	VISIT 1 DAY 0	13		
		VISIT 2 DAY 28	13		
D-TIV-YB	UNPRIMED	VISIT 1 DAY 0	287		
					Lost to follow-up
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
					Consent withdrawal, not due to an adverse event
		VISIT 2 DAY 28	281		
					Migrated / moved from the study area
					Consent withdrawal, not due to an adverse event
		VISIT 3 DAY 56	279		
	PRIM	VISIT 1 DAY 0	15		
		VISIT 2 DAY 28	15		

Group	Sub-group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
				(b) (6)	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
UNPRIMED = Unprimed subjects
PRIM = Primed subjects
N = Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

Table 43 Summary of demographic characteristics (By priming status - Total Vaccinated cohort)

		Q-QIV				D-TIV-YB				Total			
		UNPRIM N = 286		PRIM N = 13		UNPRIM N = 287		PRIM N = 15		UNPRIM N = 573		PRIM N = 28	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	17.8	-	26.8	-	17.6	-	27.0	-	17.7	-	26.9	-
	SD	8.06	-	5.52	-	8.20	-	5.69	-	8.12	-	5.51	-
	Median	16.0	-	27.0	-	16.0	-	29.0	-	16.0	-	27.5	-
	Minimum	6	-	18	-	6	-	16	-	6	-	16	-
	Maximum	35	-	34	-	35	-	34	-	35	-	34	-
Gender	Female	147	51.4	8	61.5	140	48.8	6	40.0	287	50.1	14	50.0
	Male	139	48.6	5	38.5	147	51.2	9	60.0	286	49.9	14	50.0
Ethnicity	American hispanic or latino	230	80.4	1	7.7	232	80.8	1	6.7	462	80.6	2	7.1
	Not american hispanic or latino	56	19.6	12	92.3	55	19.2	14	93.3	111	19.4	26	92.9
Geographic Ancestry	African heritage / african american	4	1.4	0	0.0	2	0.7	0	0.0	6	1.0	0	0.0
	American indian or alaskan native	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - central / south asian heritage	16	5.6	0	0.0	14	4.9	0	0.0	30	5.2	0	0.0
	Asian - east asian heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	0	0.0	0	0.0	2	0.7	0	0.0	2	0.3	0	0.0
	Native hawaiian or other pacific islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - arabic / north african heritage	0	0.0	1	7.7	0	0.0	0	0.0	0	0.0	1	3.6
	White - caucasian / european heritage	35	12.2	12	92.3	38	13.2	14	93.3	73	12.7	26	92.9
	Other	231	80.8	0	0.0	231	80.5	1	6.7	462	80.6	1	3.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter; SD = standard deviation

Table 44 Summary of demographic characteristics (By priming status - ATP cohort for immunogenicity)

		Q-QIV				D-TIV-YB				Total			
		UNPRIM N = 272		PRIM N = 12		UNPRIM N = 272		PRIM N = 15		UNPRIM N = 544		PRIM N = 27	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	17.7	-	26.8	-	17.7	-	27.0	-	17.7	-	26.9	-
	SD	8.11	-	5.75	-	8.18	-	5.69	-	8.14	-	5.61	-
	Median	16.0	-	26.0	-	16.0	-	29.0	-	16.0	-	27.0	-
	Minimum	6	-	18	-	6	-	16	-	6	-	16	-
	Maximum	35	-	34	-	35	-	34	-	35	-	34	-
Gender	Female	142	52.2	7	58.3	133	48.9	6	40.0	275	50.6	13	48.1
	Male	130	47.8	5	41.7	139	51.1	9	60.0	269	49.4	14	51.9
Ethnicity	American hispanic or latino	222	81.6	1	8.3	222	81.6	1	6.7	444	81.6	2	7.4
	Not american hispanic or latino	50	18.4	11	91.7	50	18.4	14	93.3	100	18.4	25	92.6
Geographic Ancestry	African heritage / african american	4	1.5	0	0.0	2	0.7	0	0.0	6	1.1	0	0.0
	American indian or alaskan native	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - central / south asian heritage	15	5.5	0	0.0	13	4.8	0	0.0	28	5.1	0	0.0
	Asian - east asian heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - japanese heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - south east asian heritage	0	0.0	0	0.0	2	0.7	0	0.0	2	0.4	0	0.0
	Native hawaiian or other pacific islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - arabic / north african heritage	0	0.0	1	8.3	0	0.0	0	0.0	0	0.0	1	3.7
	White - caucasian / european heritage	30	11.0	11	91.7	33	12.1	14	93.3	63	11.6	25	92.6
	Other	223	82.0	0	0.0	222	81.6	1	6.7	445	81.8	1	3.7

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 45 Age (in months) at vaccination Dose 1 by gender (By priming status - Total Vaccinated cohort)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	UNPRIM	F	147	147	17.7	7.74	6	35
		M	139	139	17.8	8.41	6	35
		Total	286	286	17.8	8.06	6	35
	PRIM	F	8	8	25.3	5.55	18	34
		M	5	5	29.4	4.93	22	34
		Total	13	13	26.8	5.52	18	34
D-TIV-YB	UNPRIM	F	140	140	18.0	8.56	6	35
		M	147	147	17.2	7.85	6	35
		Total	287	287	17.6	8.20	6	35
	PRIM	F	6	6	25.7	5.13	20	32
		M	9	9	27.9	6.17	16	34
		Total	15	15	27.0	5.69	16	34
ALL	UNPRIM	F	287	287	17.8	8.14	6	35
		M	286	286	17.5	8.12	6	35
		Total	573	573	17.7	8.12	6	35
	PRIM	F	14	14	25.4	5.17	18	34
		M	14	14	28.4	5.61	16	34
		Total	28	28	26.9	5.51	16	34

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age= number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 46 Age (in months) at vaccination Dose 1 by gender (By priming status - ATP cohort for immunogenicity)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	UNPRIM	F	142	142	17.7	7.73	6	35
		M	130	130	17.8	8.53	6	35
		Total	272	272	17.7	8.11	6	35
	PRIM	F	7	7	24.9	5.87	18	34
		M	5	5	29.4	4.93	22	34
		Total	12	12	26.8	5.75	18	34
D-TIV-YB	UNPRIM	F	133	133	17.8	8.44	6	35
		M	139	139	17.5	7.95	6	35
		Total	272	272	17.7	8.18	6	35
	PRIM	F	6	6	25.7	5.13	20	32
		M	9	9	27.9	6.17	16	34
		Total	15	15	27.0	5.69	16	34
ALL	UNPRIM	F	275	275	17.7	8.07	6	35
		M	269	269	17.7	8.23	6	35
		Total	544	544	17.7	8.14	6	35
	PRIM	F	13	13	25.2	5.33	18	34
		M	14	14	28.4	5.61	16	34
		Total	27	27	26.9	5.61	16	34

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age= number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

10.2. Immunogenicity results

10.2.1. ATP cohort for immunogenicity

10.2.1.1. Overall

Table 47 Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (ATP cohort for immunogenicity)

				≥ 10 1/DIL				GMT				
						95% CI			95% CI			
Strain	Group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	PRE	284	60	21.1	16.5	26.3	9.6	8.1	11.3	<10.0	1810.0
		POST	284	276	97.2	94.5	98.8	157.1	132.8	185.9	<10.0	5120.0
	D-TIV-YB	PRE	287	59	20.6	16.0	25.7	9.8	8.3	11.6	<10.0	905.0
		POST	287	240	83.6	78.8	87.7	61.2	49.2	76.2	<10.0	3620.0
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	PRE	284	101	35.6	30.0	41.4	17.4	14.1	21.5	<10.0	1280.0
		POST	284	275	96.8	94.1	98.5	159.4	129.4	196.3	<10.0	3620.0
	D-TIV-YB	PRE	287	89	31.0	25.7	36.7	13.8	11.4	16.8	<10.0	1280.0
		POST	287	274	95.5	92.4	97.6	103.0	83.7	126.7	<10.0	3620.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	PRE	284	62	21.8	17.2	27.1	7.7	6.9	8.7	<10.0	320.0
		POST	284	280	98.6	96.4	99.6	114.2	100.0	130.5	<10.0	1810.0
	D-TIV-YB	PRE	287	58	20.2	15.7	25.3	7.2	6.5	8.0	<10.0	905.0
		POST	287	280	97.6	95.0	99.0	107.2	92.2	124.6	<10.0	2560.0
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	PRE	284	87	30.6	25.3	36.4	10.6	9.1	12.4	<10.0	640.0
		POST	284	275	96.8	94.1	98.5	111.4	91.9	135.2	<10.0	5120.0
	D-TIV-YB	PRE	287	73	25.4	20.5	30.9	9.3	8.0	10.7	<10.0	905.0
		POST	287	153	53.3	47.4	59.2	15.6	13.3	18.5	<10.0	1280.0

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results; n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 48 Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (ATP cohort for immunogenicity)

				SPR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	PRE	284	46	16.2	12.1	21.0
		POST	284	254	89.4	85.3	92.8
	D-TIV-YB	PRE	287	47	16.4	12.3	21.2
		POST	287	169	58.9	53.0	64.6
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	PRE	284	93	32.7	27.3	38.5
		POST	284	231	81.3	76.3	85.7
	D-TIV-YB	PRE	287	74	25.8	20.8	31.3
		POST	287	191	66.6	60.8	72.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	PRE	284	26	9.2	6.1	13.1
		POST	284	242	85.2	80.5	89.1
	D-TIV-YB	PRE	287	24	8.4	5.4	12.2
		POST	287	229	79.8	74.7	84.3
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	PRE	284	56	19.7	15.3	24.8
		POST	284	216	76.1	70.7	80.9
	D-TIV-YB	PRE	287	45	15.7	11.7	20.4
		POST	287	74	25.8	20.8	31.3

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
SPR = seroprotection rate
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 49 Mean geometric increase (MGI) for HI antibodies against Flu A/CAL/7/09, Flu A/Victoria/361/11, Flu B/Bri/60/08 and Flu B/Hubei-Wujiagang/158/09 28 days after last vaccine dose (ATP cohort for immunogenicity)

			MGI		
				95% CI	
Strain	Group	N	Value	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab (1/DIL)	Q-QIV	284	16.4	14.3	18.7
	D-TIV-YB	287	6.2	5.3	7.3
Flu A/Victoria/361/11 (H3N2). HA Ab (1/DIL)	Q-QIV	284	9.1	8.0	10.5
	D-TIV-YB	287	7.5	6.4	8.7
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab (1/DIL)	Q-QIV	284	14.8	12.8	17.1
	D-TIV-YB	287	14.8	12.8	17.2
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Q-QIV	284	10.5	9.2	11.9
	D-TIV-YB	287	1.7	1.5	1.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = Number of subjects with pre- and post-vaccination results available
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 50 Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab 28 days after last vaccine dose (ATP cohort for immunogenicity)

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	284	244	85.9	81.3	89.7
	D-TIV-YB	287	154	53.7	47.7	59.5
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	284	205	72.2	66.6	77.3
	D-TIV-YB	287	160	55.7	49.8	61.6
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	284	224	78.9	73.7	83.5
	D-TIV-YB	287	222	77.4	72.1	82.1
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	284	210	73.9	68.4	79.0
	D-TIV-YB	287	28	9.8	6.6	13.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 51 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (ATP cohort for immunogenicity)

				Adjusted GMT ratio (Q-QIV / D-TIV-YB)		
Q-QIV		**D-TIV-YB**			**95% CI**	
N	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
284	104.6	287	16.7	6.28	5.32	7.41

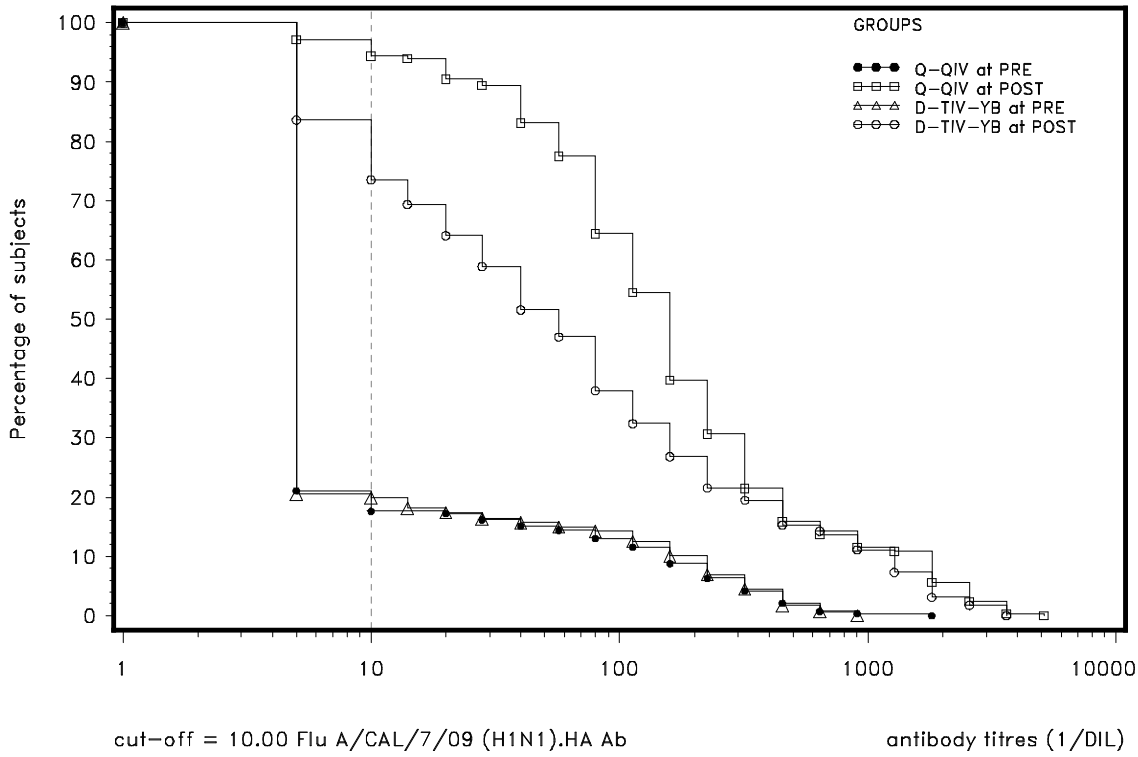
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 52 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (ATP cohort for immunogenicity)

								Difference in SCR (Q-QIV minus D-TIV-YB)		
		Q-QIV			D-TIV-YB				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria).HA Ab (1/DIL)	Total	284	210	73.9	287	28	9.8	64.19	57.65	69.95

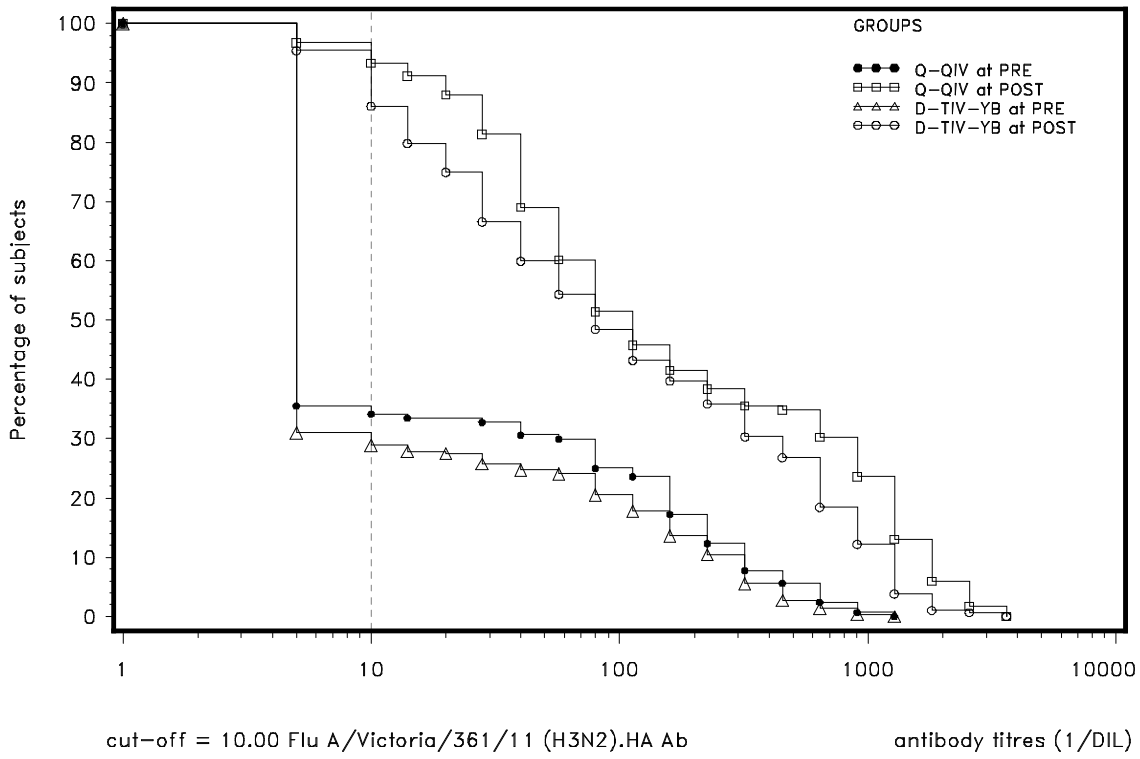
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Figure 2 Reverse cumulative distribution curves for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab at Day 0 and 28 days after the last vaccination (ATP cohort for immunogenicity)



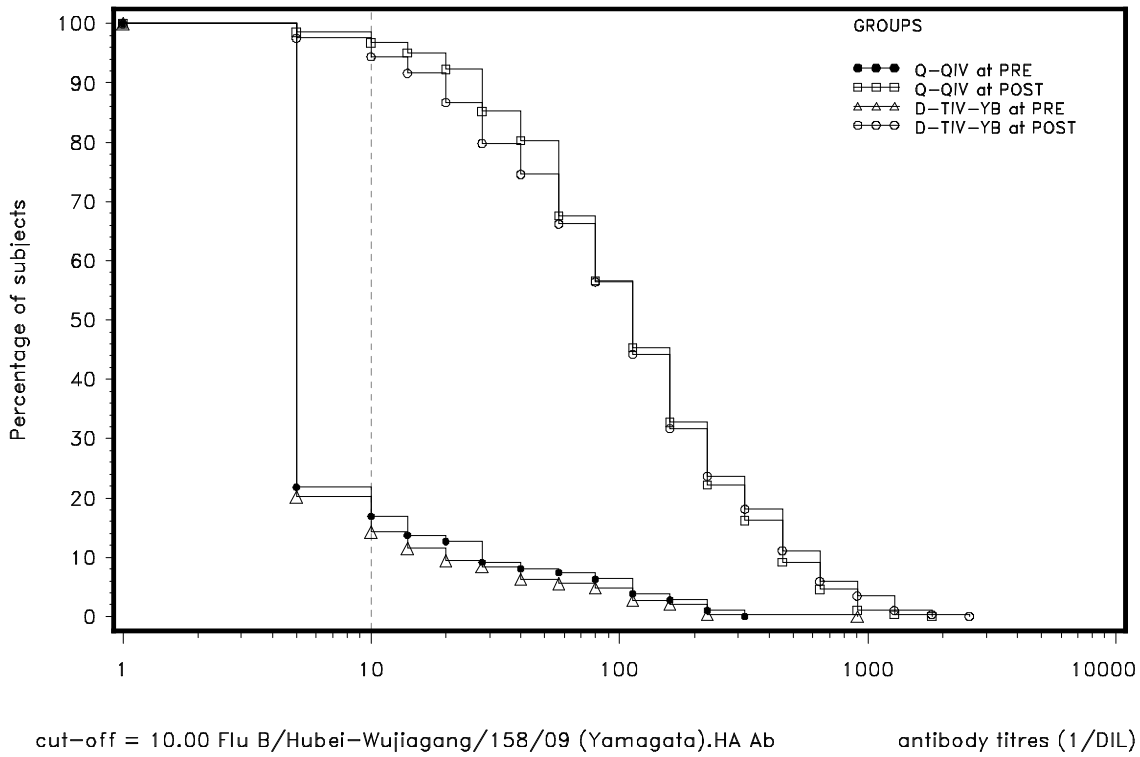
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 3 Reverse cumulative distribution curves for HI antibodies against Flu A/Victoria/361/11 (H3N2). HA Ab at Day 0 and 28 days after the last vaccination (ATP cohort for immunogenicity)



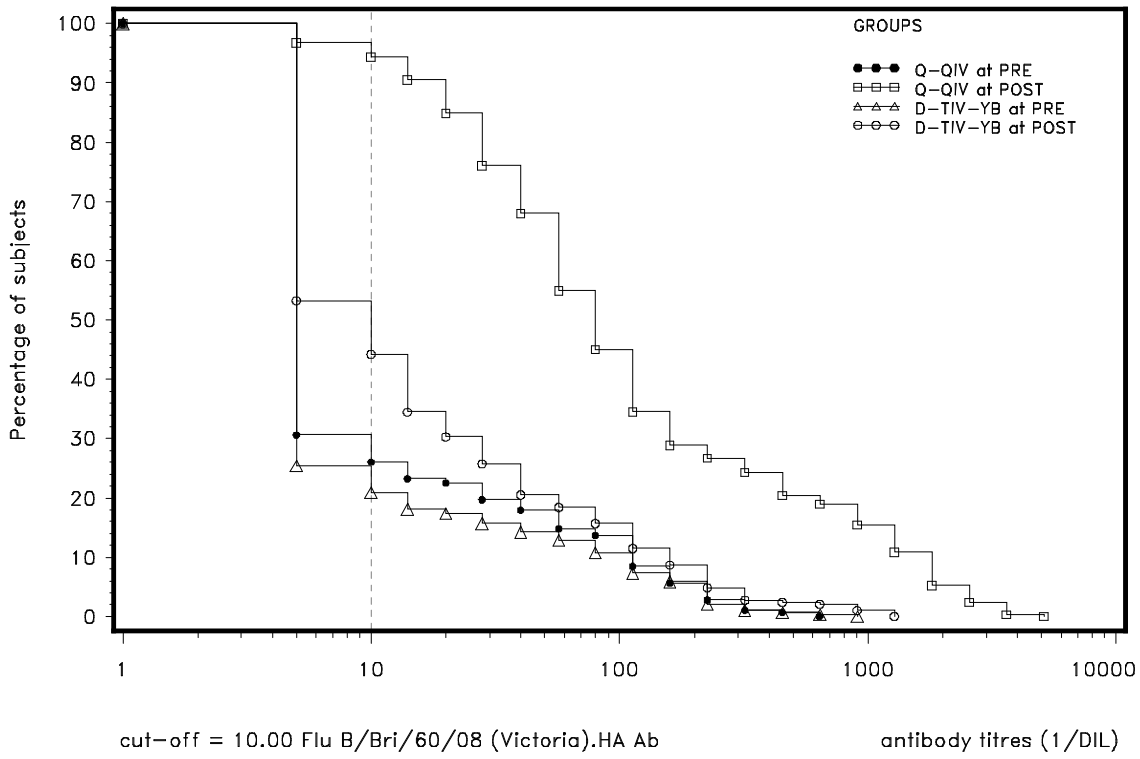
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 4 Reverse cumulative distribution curves for HI antibodies against Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab at Day 0 and 28 days after the last vaccination (ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 5 Reverse cumulative distribution curves for HI antibodies against Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after the last vaccination (ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

10.2.1.2. By age strata

Table 53 Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (H1N1).HA Ab, Flu A/Victoria/361/11 (H3N2).HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT				
							95% CI			95% CI			
Strain	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	6-17M	PRE	151	19	12.6	7.7	19.0	7.0	5.9	8.3	<10.0	1810.0
			POST	151	143	94.7	89.8	97.7	103.2	82.2	129.5	<10.0	5120.0
		18-35M	PRE	133	41	30.8	23.1	39.4	13.7	10.3	18.3	<10.0	640.0
			POST	133	133	100	97.3	100	253.2	201.7	317.7	10.0	3620.0
	D-TIV-YB	6-17M	PRE	149	15	10.1	5.7	16.1	6.9	5.8	8.2	<10.0	640.0
			POST	149	111	74.5	66.7	81.3	28.6	21.7	37.7	<10.0	3620.0
		18-35M	PRE	138	44	31.9	24.2	40.4	14.4	10.8	19.1	<10.0	905.0
			POST	138	129	93.5	88.0	97.0	139.3	104.1	186.4	<10.0	3620.0
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	6-17M	PRE	151	38	25.2	18.5	32.9	12.4	9.5	16.1	<10.0	1280.0
			POST	151	143	94.7	89.8	97.7	108.3	81.0	144.8	<10.0	3620.0
		18-35M	PRE	133	63	47.4	38.7	56.2	25.6	18.4	35.7	<10.0	1280.0
			POST	133	132	99.2	95.9	100	247.1	185.9	328.6	<10.0	3620.0
	D-TIV-YB	6-17M	PRE	149	26	17.4	11.7	24.5	9.2	7.3	11.6	<10.0	905.0
			POST	149	141	94.6	89.7	97.7	53.5	40.9	70.1	<10.0	2560.0
		18-35M	PRE	138	63	45.7	37.2	54.3	21.4	15.9	29.0	<10.0	1280.0
			POST	138	133	96.4	91.7	98.8	208.7	158.4	274.9	<10.0	3620.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	6-17M	PRE	151	27	17.9	12.1	24.9	7.5	6.4	8.8	<10.0	320.0
			POST	151	149	98.7	95.3	99.8	93.3	78.2	111.3	<10.0	905.0
		18-35M	PRE	133	35	26.3	19.1	34.7	8.0	6.8	9.4	<10.0	226.0
			POST	133	131	98.5	94.7	99.8	143.8	118.2	174.8	<10.0	1810.0
	D-TIV-YB	6-17M	PRE	149	28	18.8	12.9	26.0	6.9	6.0	7.9	<10.0	905.0
			POST	149	144	96.6	92.3	98.9	71.8	59.0	87.5	<10.0	1810.0
		18-35M	PRE	138	30	21.7	15.2	29.6	7.7	6.5	9.0	<10.0	226.0
			POST	138	136	98.6	94.9	99.8	165.3	134.1	203.7	<10.0	2560.0
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	6-17M	PRE	151	25	16.6	11.0	23.5	6.9	6.0	7.9	<10.0	453.0
			POST	151	143	94.7	89.8	97.7	66.6	53.0	83.6	<10.0	2560.0
		18-35M	PRE	133	62	46.6	37.9	55.5	17.4	13.4	22.7	<10.0	640.0
			POST	133	132	99.2	95.9	100	200.1	149.2	268.3	<10.0	5120.0
	D-TIV-YB	6-17M	PRE	149	13	8.7	4.7	14.5	5.6	5.2	6.0	<10.0	226.0
			POST	149	54	36.2	28.5	44.5	8.6	7.4	9.9	<10.0	320.0
		18-35M	PRE	138	60	43.5	35.1	52.2	16.1	12.4	21.0	<10.0	905.0
			POST	138	99	71.7	63.5	79.1	29.9	22.8	39.2	<10.0	1280.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 54 Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	6-17M	PRE	151	11	7.3	3.7	12.7
			POST	151	125	82.8	75.8	88.4
		18-35M	PRE	133	35	26.3	19.1	34.7
			POST	133	129	97.0	92.5	99.2
	D-TIV-YB	6-17M	PRE	149	12	8.1	4.2	13.6
			POST	149	59	39.6	31.7	47.9
		18-35M	PRE	138	35	25.4	18.3	33.5
			POST	138	110	79.7	72.0	86.1
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	6-17M	PRE	151	37	24.5	17.9	32.2
			POST	151	115	76.2	68.6	82.7
		18-35M	PRE	133	56	42.1	33.6	51.0
			POST	133	116	87.2	80.3	92.4
	D-TIV-YB	6-17M	PRE	149	22	14.8	9.5	21.5
			POST	149	75	50.3	42.0	58.6
		18-35M	PRE	138	52	37.7	29.6	46.3
			POST	138	116	84.1	76.9	89.7
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	6-17M	PRE	151	13	8.6	4.7	14.3
			POST	151	123	81.5	74.3	87.3
		18-35M	PRE	133	13	9.8	5.3	16.1
			POST	133	119	89.5	83.0	94.1
	D-TIV-YB	6-17M	PRE	149	10	6.7	3.3	12.0
			POST	149	107	71.8	63.9	78.9
		18-35M	PRE	138	14	10.1	5.7	16.4
			POST	138	122	88.4	81.9	93.2
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	6-17M	PRE	151	10	6.6	3.2	11.8
			POST	151	103	68.2	60.1	75.5
		18-35M	PRE	133	46	34.6	26.6	43.3
			POST	133	113	85.0	77.7	90.6
	D-TIV-YB	6-17M	PRE	149	2	1.3	0.2	4.8
			POST	149	13	8.7	4.7	14.5
		18-35M	PRE	138	43	31.2	23.6	39.6
			POST	138	61	44.2	35.8	52.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
SPR = seroprotection rate
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 55 Mean geometric increase (MGI) for HI antibodies against Flu A/CAL/7/09, Flu A/Victoria/361/11, Flu B/Bri/60/08 and Flu B/Hubei-Wujiagang/158/09 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

				MGI		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09 (H1N1). HA Ab (1/DIL)	Q-QIV	6-17M	151	14.8	12.1	18.1
		18-35M	133	18.4	15.6	21.8
	D-TIV-YB	6-17M	149	4.1	3.4	5.1
		18-35M	138	9.7	7.8	12.0
Flu A/Victoria/361/11 (H3N2). HA Ab (1/DIL)	Q-QIV	6-17M	151	8.7	7.3	10.5
		18-35M	133	9.6	7.9	11.8
	D-TIV-YB	6-17M	149	5.8	4.8	7.1
		18-35M	138	9.7	7.7	12.2
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab (1/DIL)	Q-QIV	6-17M	151	12.5	10.2	15.3
		18-35M	133	18.0	14.6	22.1
	D-TIV-YB	6-17M	149	10.5	8.6	12.7
		18-35M	138	21.5	17.4	26.6
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Q-QIV	6-17M	151	9.7	7.9	11.8
		18-35M	133	11.5	9.8	13.4
	D-TIV-YB	6-17M	149	1.5	1.3	1.8
		18-35M	138	1.9	1.6	2.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = Number of subjects with pre- and post-vaccination results available
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 56 Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	6-17M	151	122	80.8	73.6	86.7
		18-35M	133	122	91.7	85.7	95.8
	D-TIV-YB	6-17M	149	57	38.3	30.4	46.6
		18-35M	138	97	70.3	61.9	77.8
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	6-17M	151	109	72.2	64.3	79.2
		18-35M	133	96	72.2	63.7	79.6
	D-TIV-YB	6-17M	149	63	42.3	34.2	50.6
		18-35M	138	97	70.3	61.9	77.8
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	6-17M	151	112	74.2	66.4	80.9
		18-35M	133	112	84.2	76.9	90.0
	D-TIV-YB	6-17M	149	102	68.5	60.3	75.8
		18-35M	138	120	87.0	80.2	92.1
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	6-17M	151	101	66.9	58.8	74.3
		18-35M	133	109	82.0	74.4	88.1
	D-TIV-YB	6-17M	149	11	7.4	3.7	12.8
		18-35M	138	17	12.3	7.3	19.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 57 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

				Adjusted GMT ratio (Q-QIV/6-17M / D-TIV-YB/6-17M)		
Q-QIV/6-17M		D-TIV-YB/6-17M			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
151	61.3	149	9.3	6.57	5.15	8.39

D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 58 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

				Adjusted GMT ratio (Q-QIV/18-35M / D-TIV-YB/18-35M)		
Q-QIV/18-35M		D-TIV-YB/18-35M			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
133	193.3	138	30.9	6.25	5.03	7.77

D-TIV-YB = *Fluarix* Vaccine; 18-35M = 18-35 months old subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 59 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

								Difference in SCR (Q-QIV/6-17M minus D-TIV-YB/6-17M)		
		Q-QIV/6-17M			D-TIV-YB/6-17M				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	151	101	66.9	149	11	7.4	59.50	50.33	67.50

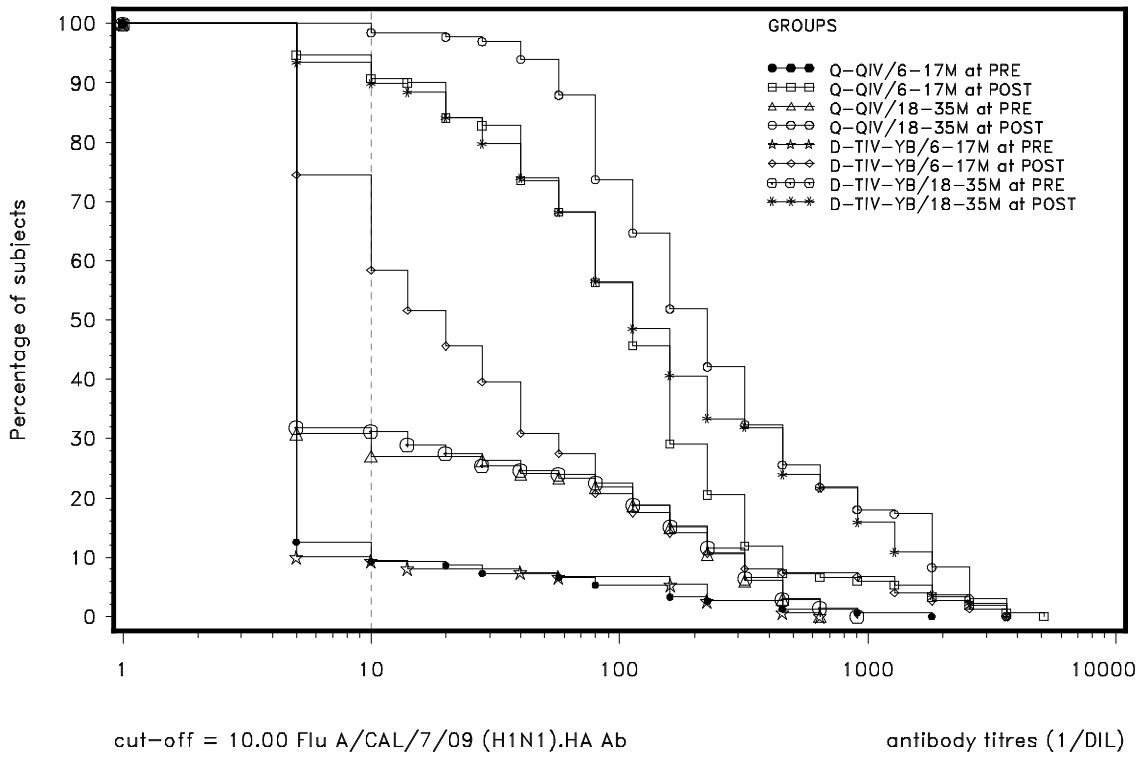
Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine; 6-17M = 6-17 months old subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 60 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - ATP cohort for immunogenicity)

								Difference in SCR (Q-QIV/18-35M minus D-TIV-YB/18-35M)		
		Q-QIV/18-35M			D-TIV-YB/18-35M				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	133	109	82.0	138	17	12.3	69.64	60.13	77.21

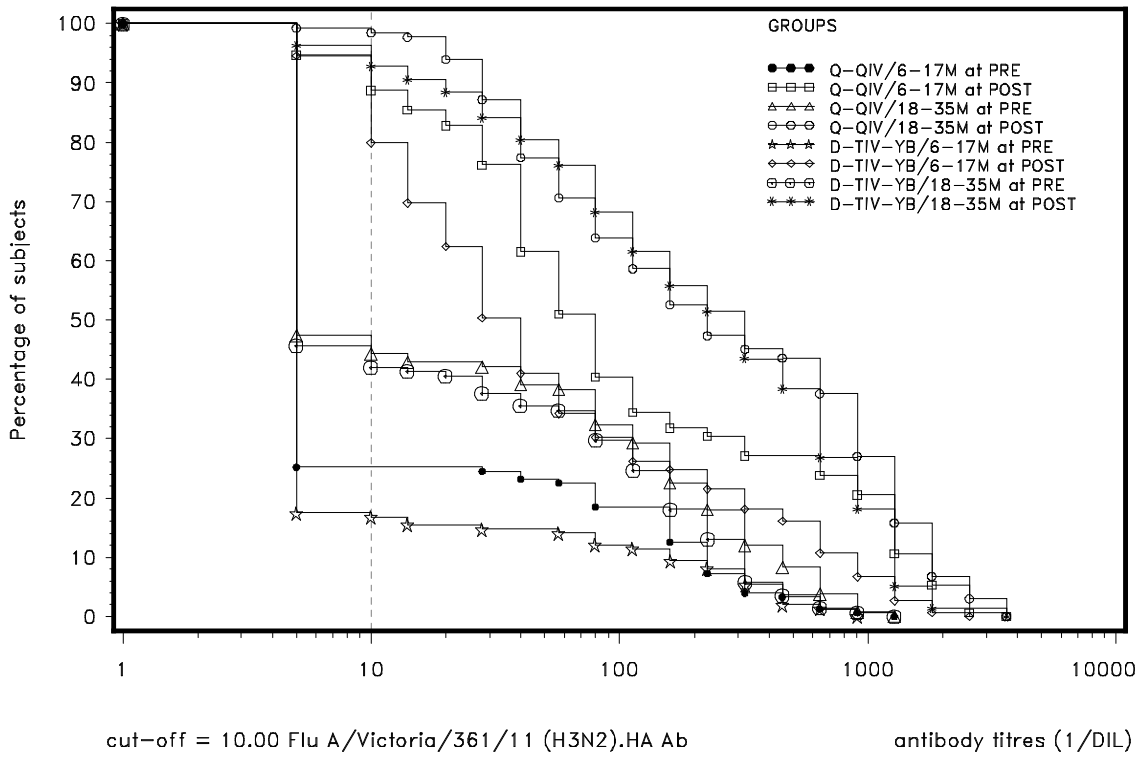
Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine; 18-35M = 18-35 months old subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Figure 6 Reverse cumulative distribution curves for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - ATP cohort for immunogenicity)



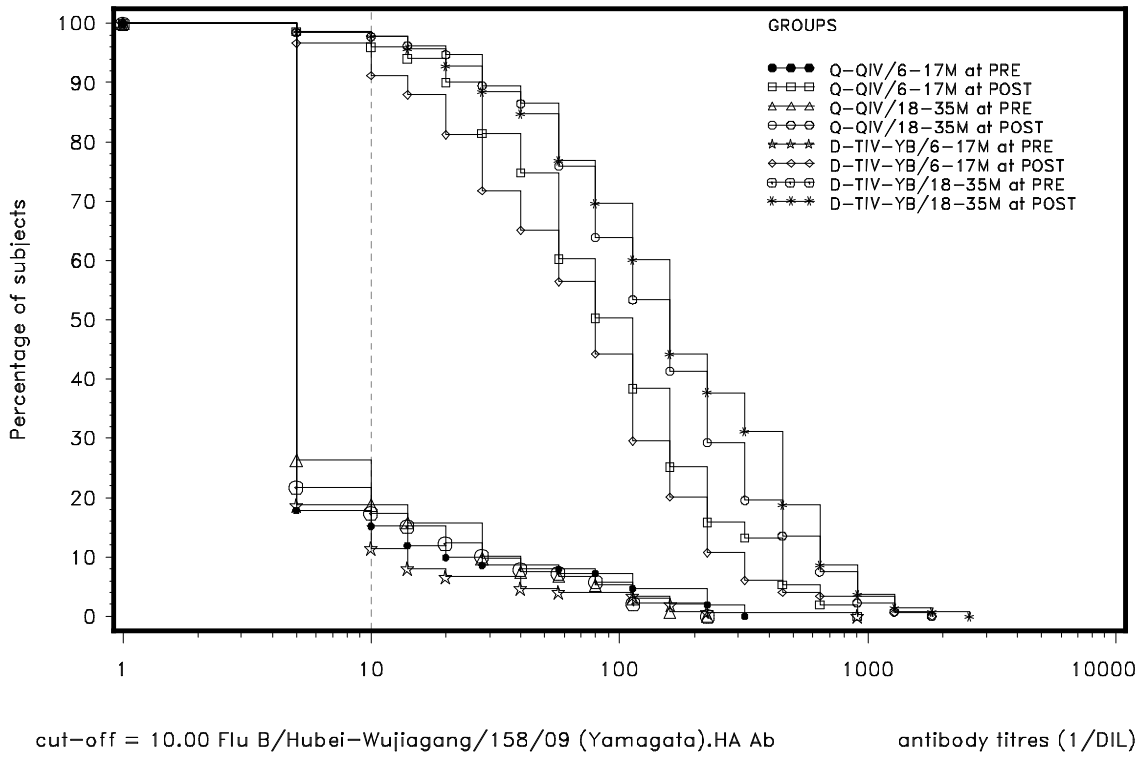
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 7 Reverse cumulative distribution curves for HI antibodies against Flu A/Victoria/361/11 (H3N2). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - ATP cohort for immunogenicity)



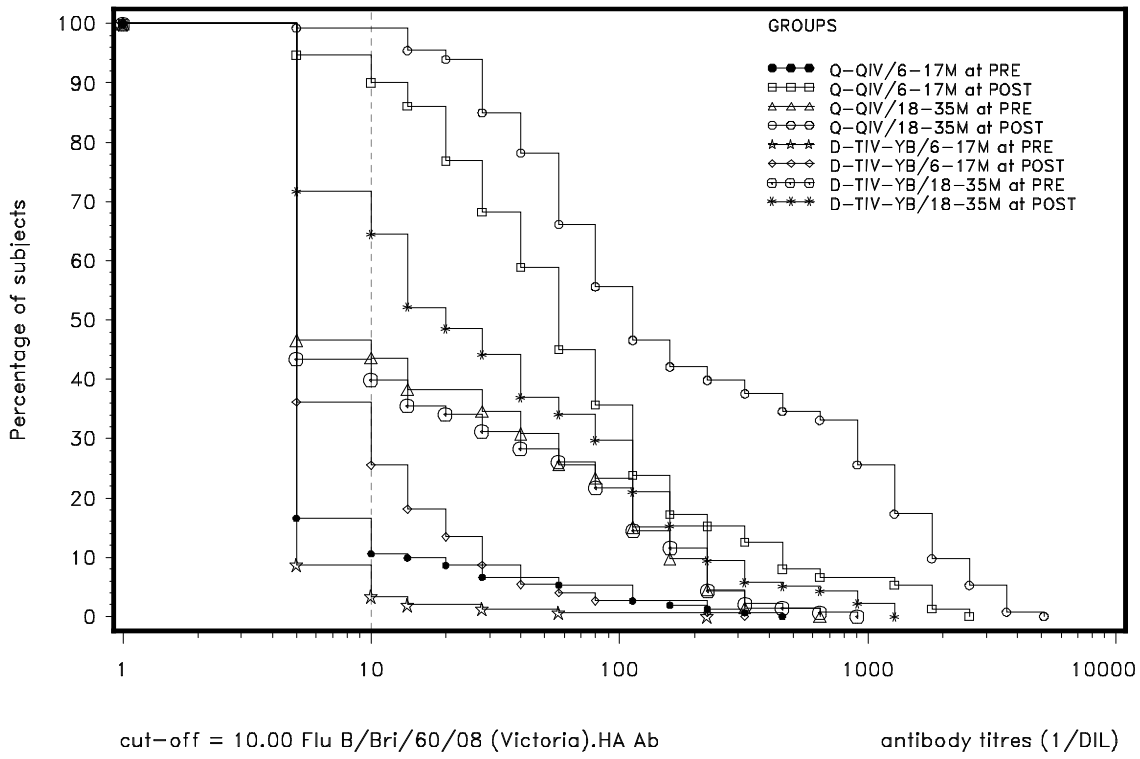
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 8 Reverse cumulative distribution curves for HI antibodies against Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 9 Reverse cumulative distribution curves for HI antibodies against Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

10.2.1.3. By priming status

Table 61 Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT				
							95% CI			95% CI			
Strain	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	UNPRIM	PRE	272	54	19.9	15.3	25.1	9.6	8.1	11.4	<10.0	1810.0
			POST	272	264	97.1	94.3	98.7	162.3	136.5	192.9	<10.0	5120.0
		PRIM	PRE	12	6	50.0	21.1	78.9	9.2	5.4	15.6	<10.0	57.0
			POST	12	12	100	73.5	100	75.5	37.6	151.3	10.0	453.0
	D-TIV-YB	UNPRIM	PRE	272	55	20.2	15.6	25.5	9.8	8.3	11.7	<10.0	905.0
			POST	272	226	83.1	78.1	87.3	60.4	48.2	75.7	<10.0	3620.0
		PRIM	PRE	15	4	26.7	7.8	55.1	9.1	4.2	19.6	<10.0	905.0
			POST	15	14	93.3	68.1	99.8	78.1	27.0	225.9	<10.0	3620.0
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	UNPRIM	PRE	272	100	36.8	31.0	42.8	18.1	14.6	22.5	<10.0	1280.0
			POST	272	263	96.7	93.8	98.5	167.7	135.4	207.7	<10.0	3620.0
		PRIM	PRE	12	1	8.3	0.2	38.5	7.1	3.3	15.2	<10.0	320.0
			POST	12	12	100	73.5	100	50.4	23.4	108.3	10.0	1280.0
	D-TIV-YB	UNPRIM	PRE	272	86	31.6	26.1	37.5	14.3	11.7	17.5	<10.0	1280.0
			POST	272	262	96.3	93.3	98.2	107.9	87.3	133.5	<10.0	3620.0
		PRIM	PRE	15	3	20.0	4.3	48.1	7.4	4.1	13.5	<10.0	320.0
			POST	15	12	80.0	51.9	95.7	43.8	17.5	109.9	<10.0	640.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	UNPRIM	PRE	272	59	21.7	16.9	27.1	7.8	6.9	8.8	<10.0	320.0
			POST	272	270	99.3	97.4	99.9	121.7	106.7	138.7	<10.0	1810.0
		PRIM	PRE	12	3	25.0	5.5	57.2	6.1	4.8	7.8	<10.0	14.0
			POST	12	10	83.3	51.6	97.9	27.4	13.1	57.3	<10.0	160.0
	D-TIV-YB	UNPRIM	PRE	272	54	19.9	15.3	25.1	7.3	6.5	8.1	<10.0	905.0
			POST	272	266	97.8	95.3	99.2	113.4	97.5	131.9	<10.0	2560.0
		PRIM	PRE	15	4	26.7	7.8	55.1	7.1	4.8	10.4	<10.0	57.0
			POST	15	14	93.3	68.1	99.8	38.9	17.4	87.0	<10.0	1280.0
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	UNPRIM	PRE	272	79	29.0	23.7	34.8	10.6	9.0	12.4	<10.0	640.0
			POST	272	263	96.7	93.8	98.5	112.8	92.3	137.8	<10.0	5120.0
		PRIM	PRE	12	8	66.7	34.9	90.1	12.2	7.2	20.8	<10.0	57.0
			POST	12	12	100	73.5	100	84.6	47.4	151.0	28.0	640.0
	D-TIV-YB	UNPRIM	PRE	272	62	22.8	17.9	28.2	8.8	7.7	10.2	<10.0	905.0
			POST	272	140	51.5	45.4	57.5	14.7	12.4	17.4	<10.0	1280.0
		PRIM	PRE	15	11	73.3	44.9	92.2	21.9	10.3	46.5	<10.0	320.0
			POST	15	13	86.7	59.5	98.3	48.0	22.2	103.9	<10.0	905.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 62 Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	UNPRIM	PRE	272	44	16.2	12.0	21.1
			POST	272	245	90.1	85.9	93.4
		PRIM	PRE	12	2	16.7	2.1	48.4
			POST	12	9	75.0	42.8	94.5
	D-TIV-YB	UNPRIM	PRE	272	46	16.9	12.7	21.9
			POST	272	161	59.2	53.1	65.1
		PRIM	PRE	15	1	6.7	0.2	31.9
			POST	15	8	53.3	26.6	78.7
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	UNPRIM	PRE	272	92	33.8	28.2	39.8
			POST	272	223	82.0	76.9	86.4
		PRIM	PRE	12	1	8.3	0.2	38.5
			POST	12	8	66.7	34.9	90.1
	D-TIV-YB	UNPRIM	PRE	272	73	26.8	21.7	32.5
			POST	272	183	67.3	61.4	72.8
		PRIM	PRE	15	1	6.7	0.2	31.9
			POST	15	8	53.3	26.6	78.7
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	UNPRIM	PRE	272	26	9.6	6.3	13.7
			POST	272	237	87.1	82.6	90.9
		PRIM	PRE	12	0	0.0	0.0	26.5
			POST	12	5	41.7	15.2	72.3
	D-TIV-YB	UNPRIM	PRE	272	23	8.5	5.4	12.4
			POST	272	224	82.4	77.3	86.7
		PRIM	PRE	15	1	6.7	0.2	31.9
			POST	15	5	33.3	11.8	61.6
Flu B/Bri/60/08 (Victoria).HA Ab	Q-QIV	UNPRIM	PRE	272	54	19.9	15.3	25.1
			POST	272	207	76.1	70.6	81.0
		PRIM	PRE	12	2	16.7	2.1	48.4
			POST	12	9	75.0	42.8	94.5
	D-TIV-YB	UNPRIM	PRE	272	41	15.1	11.0	19.9
			POST	272	65	23.9	19.0	29.4
		PRIM	PRE	15	4	26.7	7.8	55.1
			POST	15	9	60.0	32.3	83.7

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
SPR = seroprotection rate
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 63 Mean geometric increase (MGI) for HI antibodies against Flu A/CAL/7/09, Flu A/Victoria/361/11, Flu B/Bri/60/08 and Flu B/Hubei-Wujiagang/158/09 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

				MGI		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09 (H1N1). HA Ab (1/DIL)	Q-QIV	UNPRIM	272	16.9	14.7	19.3
		PRIM	12	8.2	5.1	13.3
	D-TIV-YB	UNPRIM	272	6.1	5.2	7.2
		PRIM	15	8.6	3.7	20.0
Flu A/Victoria/361/11 (H3N2). HA Ab (1/DIL)	Q-QIV	UNPRIM	272	9.2	8.0	10.6
		PRIM	12	7.1	4.7	10.9
	D-TIV-YB	UNPRIM	272	7.5	6.5	8.8
		PRIM	15	5.9	2.7	12.9
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab (1/DIL)	Q-QIV	UNPRIM	272	15.6	13.4	18.1
		PRIM	12	4.5	2.5	8.2
	D-TIV-YB	UNPRIM	272	15.6	13.4	18.2
		PRIM	15	5.5	3.3	9.3
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Q-QIV	UNPRIM	272	10.7	9.3	12.2
		PRIM	12	6.9	4.4	10.9
	D-TIV-YB	UNPRIM	272	1.7	1.5	1.9
		PRIM	15	2.2	1.4	3.5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = Number of subjects with pre- and post-vaccination results available
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 64 Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	UNPRIM	272	236	86.8	82.2	90.6
		PRIM	12	8	66.7	34.9	90.1
	D-TIV-YB	UNPRIM	272	147	54.0	47.9	60.1
		PRIM	15	7	46.7	21.3	73.4
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	UNPRIM	272	197	72.4	66.7	77.7
		PRIM	12	8	66.7	34.9	90.1
	D-TIV-YB	UNPRIM	272	153	56.3	50.1	62.2
		PRIM	15	7	46.7	21.3	73.4
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	UNPRIM	272	219	80.5	75.3	85.1
		PRIM	12	5	41.7	15.2	72.3
	D-TIV-YB	UNPRIM	272	217	79.8	74.5	84.4
		PRIM	15	5	33.3	11.8	61.6
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	UNPRIM	272	202	74.3	68.6	79.4
		PRIM	12	8	66.7	34.9	90.1
	D-TIV-YB	UNPRIM	272	26	9.6	6.3	13.7
		PRIM	15	2	13.3	1.7	40.5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 65 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

				Adjusted GMT ratio (Q-QIV/UNPRIM / D-TIV-YB/UNPRIM)		
Q-QIV/UNPRIM		D-TIV-YB/UNPRIM			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
272	103.9	272	16.0	6.51	5.49	7.72

D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 66 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

				Adjusted GMT ratio (Q-QIV/PRIM / D-TIV-YB/PRIM)		
Q-QIV/PRIM		D-TIV-YB/PRIM			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
12	109.7	15	39.0	2.81	1.48	5.34

D-TIV-YB = *Fluarix* Vaccine
PRIM = Primed subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 67 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

								Difference in SCR (Q-QIV/UNPRIM minus D-TIV-YB/UNPRIM)		
		Q-QIV/UNPRIM			D-TIV-YB/UNPRIM				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	272	202	74.3	272	26	9.6	64.71	58.03	70.55

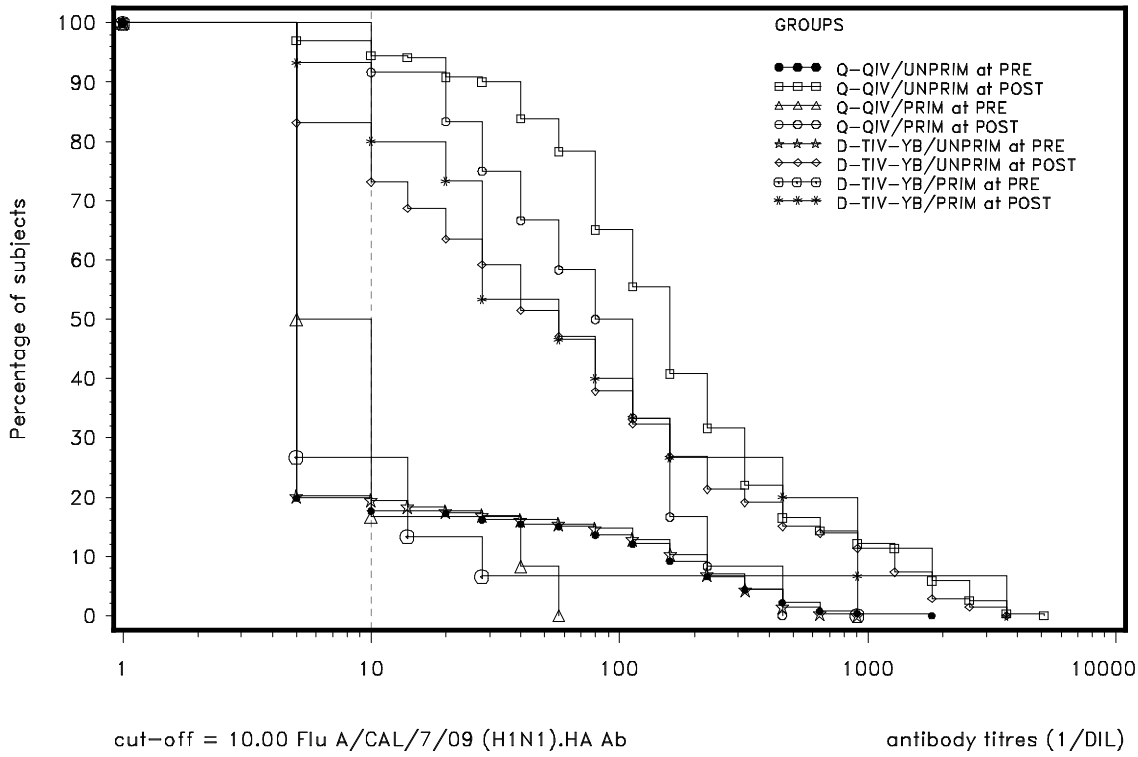
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 68 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - ATP cohort for immunogenicity)

								Difference in SCR (Q-QIV/PRIM minus D-TIV-YB/PRIM)		
		Q-QIV/PRIM			D-TIV-YB/PRIM				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	12	8	66.7	15	2	13.3	53.33	16.52	77.84

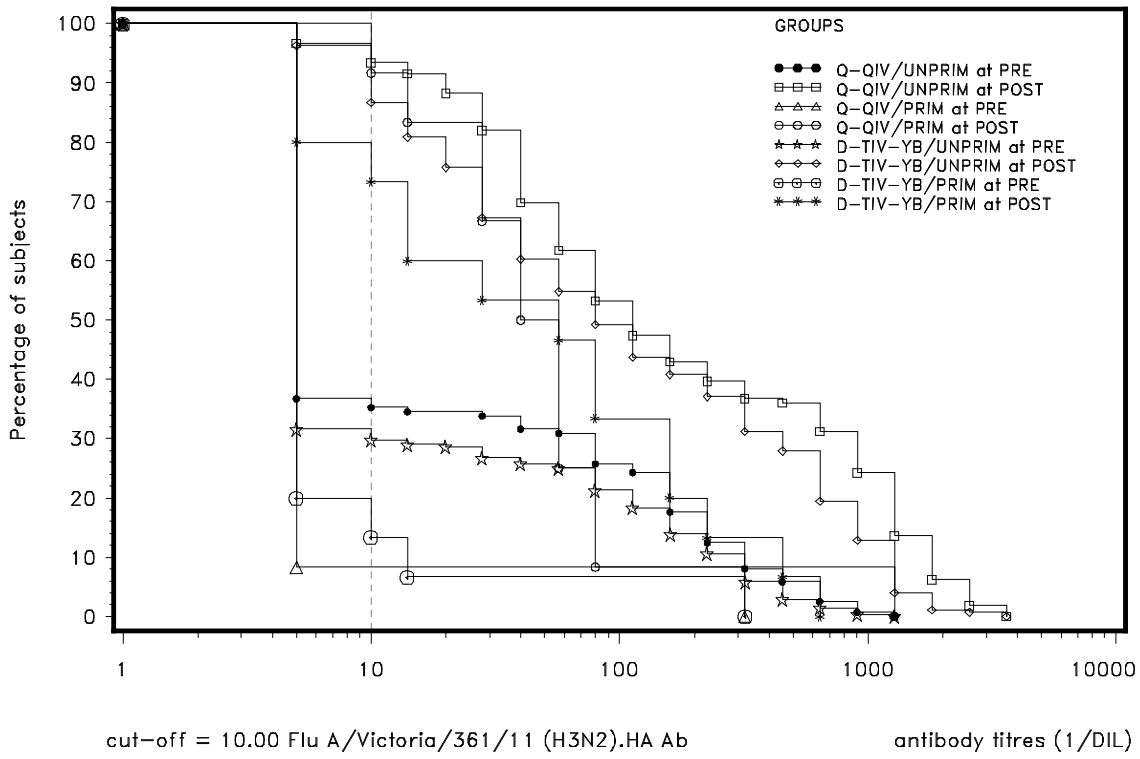
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRIM = Primed subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Figure 10 Reverse cumulative distribution curves for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - ATP cohort for immunogenicity)



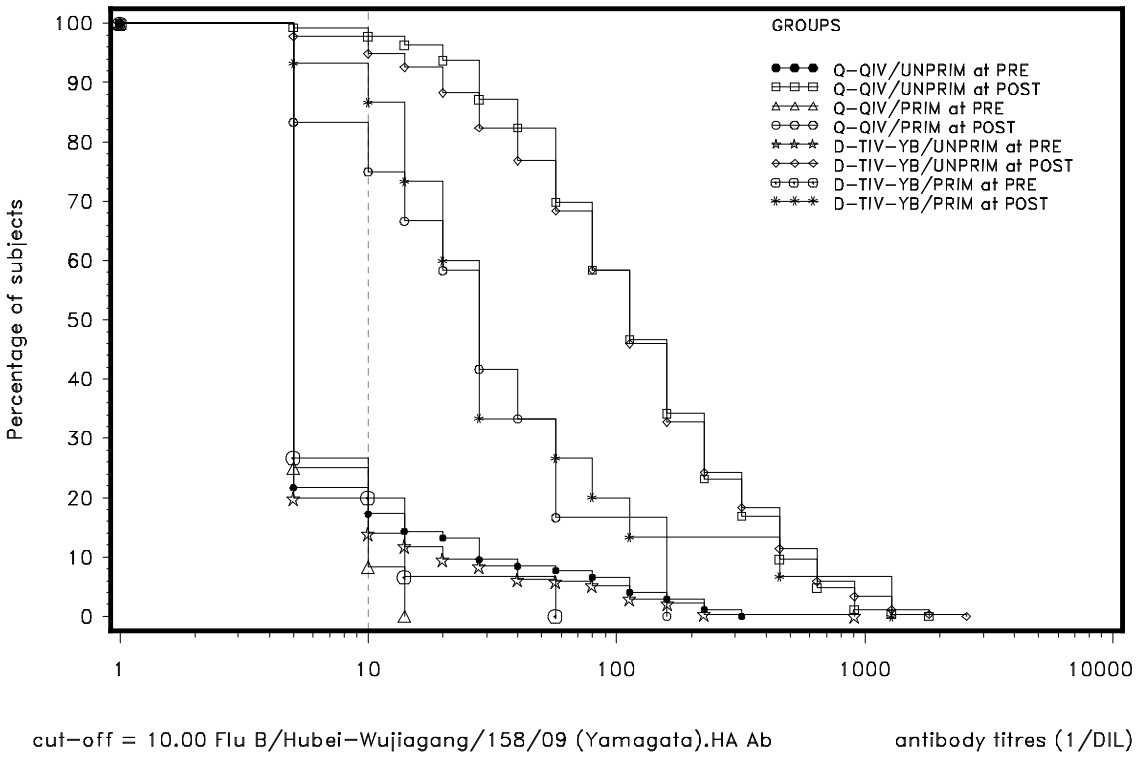
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 11 Reverse cumulative distribution curves for HI antibodies against Flu A/Victoria/361/11 (H3N2). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - ATP cohort for immunogenicity)



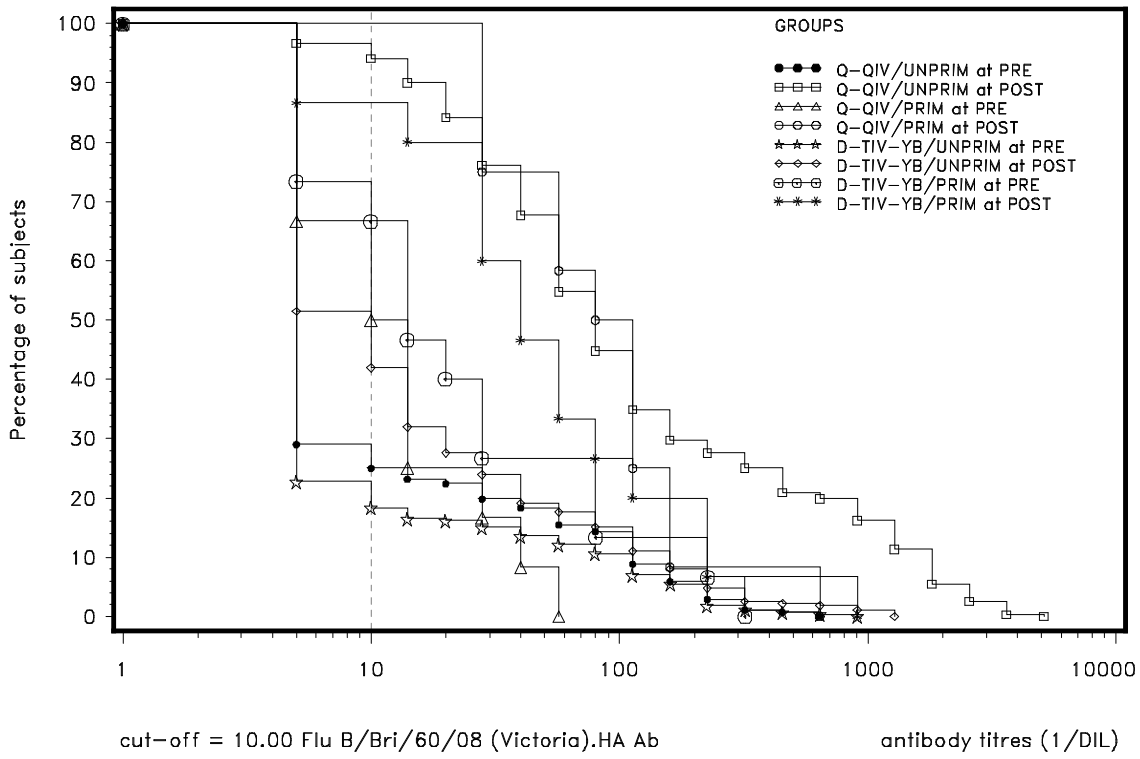
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 12 Reverse cumulative distribution curves for HI antibodies against Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - ATP cohortfor immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 13 Reverse cumulative distribution curves for HI antibodies against Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = *Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])*

10.2.2. Total Vaccinated cohort

10.2.2.1. Overall

Table 69 Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (Total Vaccinated cohort)

				≥ 10 1/DIL				GMT				
						95% CI			95% CI			
Strain	Group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	PRE	299	63	21.1	16.6	26.1	9.6	8.2	11.3	<10.0	1810.0
		POST	286	278	97.2	94.6	98.8	155.8	131.8	184.2	<10.0	5120.0
	D-TIV-YB	PRE	302	63	20.9	16.4	25.9	9.8	8.3	11.5	<10.0	905.0
		POST	293	246	84.0	79.2	88.0	63.4	51.0	78.8	<10.0	3620.0
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	PRE	299	106	35.5	30.0	41.2	17.1	14.0	21.0	<10.0	1280.0
		POST	286	277	96.9	94.1	98.6	158.0	128.4	194.5	<10.0	3620.0
	D-TIV-YB	PRE	302	93	30.8	25.6	36.3	13.7	11.4	16.5	<10.0	1280.0
		POST	293	279	95.2	92.1	97.4	103.7	84.4	127.3	<10.0	3620.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	PRE	299	67	22.4	17.8	27.6	7.8	6.9	8.7	<10.0	320.0
		POST	286	282	98.6	96.5	99.6	113.7	99.6	129.7	<10.0	1810.0
	D-TIV-YB	PRE	302	60	19.9	15.5	24.8	7.2	6.5	7.9	<10.0	905.0
		POST	293	286	97.6	95.1	99.0	107.9	93.0	125.0	<10.0	2560.0
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	PRE	299	92	30.8	25.6	36.3	10.6	9.2	12.3	<10.0	640.0
		POST	286	277	96.9	94.1	98.6	111.1	91.7	134.6	<10.0	5120.0
	D-TIV-YB	PRE	302	76	25.2	20.4	30.5	9.3	8.1	10.7	<10.0	905.0
		POST	293	157	53.6	47.7	59.4	15.7	13.3	18.6	<10.0	1280.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 70 Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (Total Vaccinated cohort)

				SPR			
						95% CI	
Strain	Group	Timing	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	PRE	299	49	16.4	12.4	21.1
		POST	286	256	89.5	85.4	92.8
	D-TIV-YB	PRE	302	49	16.2	12.3	20.9
		POST	293	175	59.7	53.9	65.4
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	PRE	299	97	32.4	27.2	38.1
		POST	286	232	81.1	76.1	85.5
	D-TIV-YB	PRE	302	77	25.5	20.7	30.8
		POST	293	196	66.9	61.2	72.3
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	PRE	299	27	9.0	6.0	12.9
		POST	286	244	85.3	80.7	89.2
	D-TIV-YB	PRE	302	24	7.9	5.2	11.6
		POST	293	235	80.2	75.2	84.6
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	PRE	299	59	19.7	15.4	24.7
		POST	286	217	75.9	70.5	80.7
	D-TIV-YB	PRE	302	48	15.9	12.0	20.5
		POST	293	76	25.9	21.0	31.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
SPR = seroprotection rate
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 71 Mean geometric increase (MGI) for HI antibodies against Flu A/CAL/7/09, Flu A/Victoria/361/11, Flu B/Bri/60/08 and Flu B/Hubei-Wujiagang/158/09 28 days after last vaccine dose (Total Vaccinated cohort)

			MGI		
				95% CI	
Strain	Group	N	Value	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab (1/DIL)	Q-QIV	286	16.3	14.3	18.6
	D-TIV-YB	293	6.3	5.4	7.4
Flu A/Victoria/361/11 (H3N2). HA Ab (1/DIL)	Q-QIV	286	9.2	8.0	10.5
	D-TIV-YB	293	7.4	6.4	8.6
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab (1/DIL)	Q-QIV	286	14.7	12.7	17.0
	D-TIV-YB	293	14.9	12.9	17.3
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Q-QIV	286	10.5	9.2	11.9
	D-TIV-YB	293	1.7	1.5	1.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = Number of subjects with pre- and post-vaccination results available
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 72 Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab 28 days after last vaccine dose (Total Vaccinated cohort)

			SCR			
					95% CI	
Strain	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	286	246	86.0	81.4	89.8
	D-TIV-YB	293	159	54.3	48.4	60.1
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	286	206	72.0	66.4	77.2
	D-TIV-YB	293	163	55.6	49.7	61.4
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	286	226	79.0	73.8	83.6
	D-TIV-YB	293	228	77.8	72.6	82.4
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	286	211	73.8	68.3	78.8
	D-TIV-YB	293	29	9.9	6.7	13.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 73 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (Total Vaccinated cohort)

				Adjusted GMT ratio (Q-QIV / D-TIV-YB)		
Q-QIV		**D-TIV-YB**			**95% CI**	
N	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
286	104.6	293	16.7	6.26	5.32	7.37

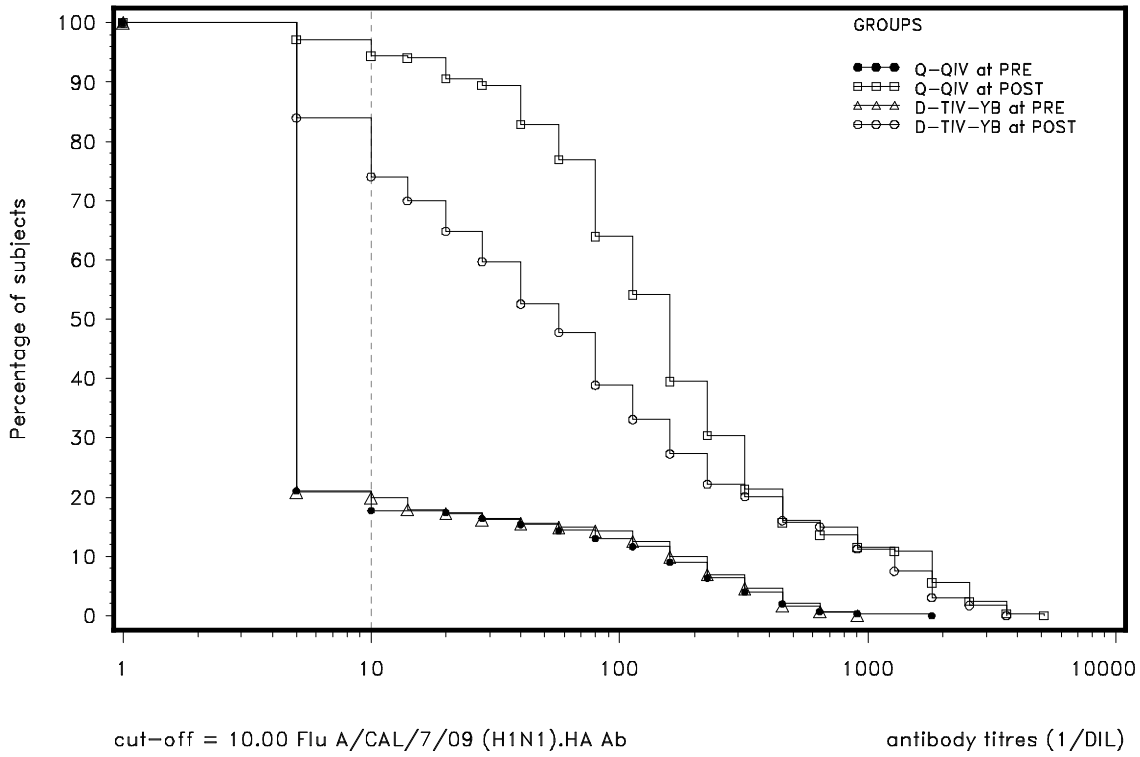
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 74 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (Total Vaccinated cohort)

								Difference in SCR (Q-QIV minus D-TIV-YB)		
		Q-QIV			D-TIV-YB				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	286	211	73.8	293	29	9.9	63.88	57.36	69.63

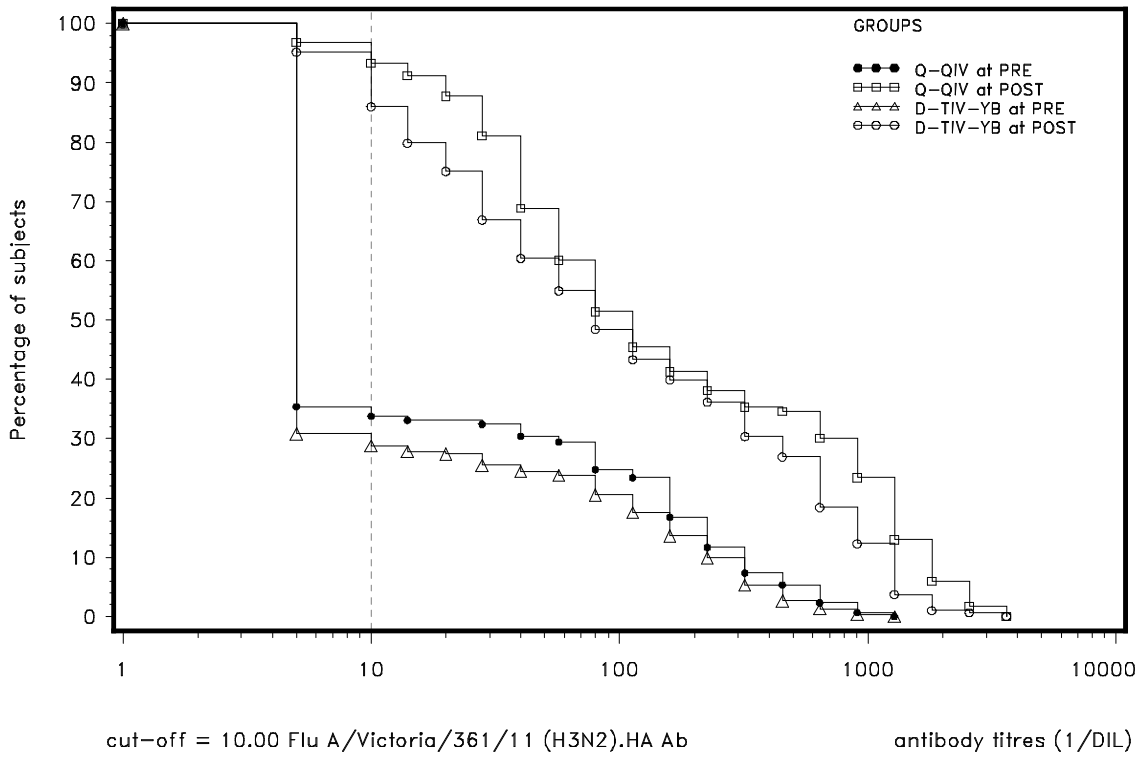
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Figure 14 Reverse cumulative distribution curves for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab at Day 0 and 28 days after the last vaccination (Total Vaccinated cohort)



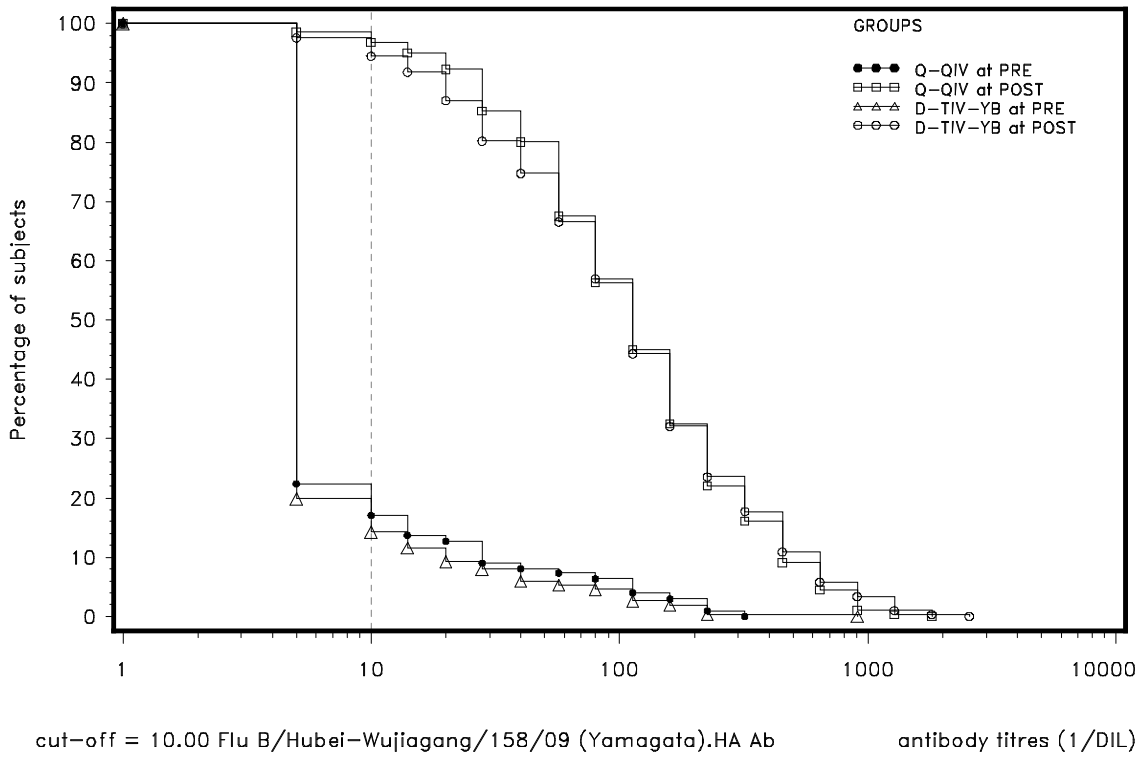
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 15 Reverse cumulative distribution curves for HI antibodies against Flu A/Victoria/361/11 (H3N2). HA Ab at Day 0 and 28 days after the last vaccination (Total Vaccinated cohort)



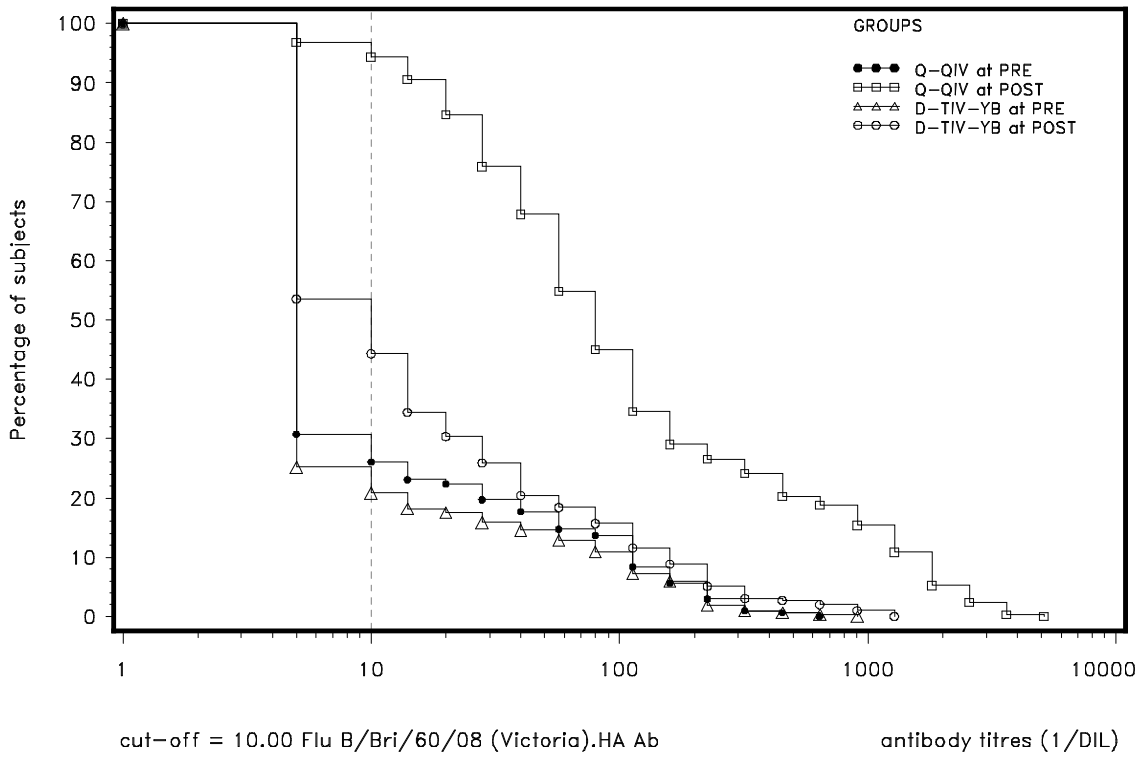
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 16 Reverse cumulative distribution curves for HI antibodies against Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab at Day 0 and 28 days after the last vaccination (Total Vaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 17 Reverse cumulative distribution curves for HI antibodies against Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after the last vaccination (Total Vaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

10.2.2.2. By age strata

Table 75 Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

					≥ 10 1/DIL				GMT				
							95% CI			95% CI			
Strain	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	6-17M	PRE	157	19	12.1	7.4	18.3	6.9	5.9	8.1	<10.0	1810.0
			POST	152	144	94.7	89.9	97.7	102.6	81.8	128.6	<10.0	5120.0
		18-35M	PRE	142	44	31.0	23.5	39.3	13.9	10.5	18.3	<10.0	640.0
			POST	134	134	100	97.3	100	250.4	199.6	314.0	10.0	3620.0
	D-TIV-YB	6-17M	PRE	160	16	10.0	5.8	15.7	6.9	5.8	8.1	<10.0	640.0
			POST	152	114	75.0	67.3	81.7	29.7	22.6	39.1	<10.0	3620.0
		18-35M	PRE	142	47	33.1	25.4	41.5	14.6	11.0	19.3	<10.0	905.0
			POST	141	132	93.6	88.2	97.0	143.6	107.6	191.6	<10.0	3620.0
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	6-17M	PRE	157	39	24.8	18.3	32.4	12.3	9.5	15.8	<10.0	1280.0
			POST	152	144	94.7	89.9	97.7	107.1	80.2	143.1	<10.0	3620.0
		18-35M	PRE	142	67	47.2	38.8	55.7	24.8	18.1	34.1	<10.0	1280.0
			POST	134	133	99.3	95.9	100	245.7	185.2	326.0	<10.0	3620.0
	D-TIV-YB	6-17M	PRE	160	28	17.5	12.0	24.3	9.2	7.4	11.5	<10.0	905.0
			POST	152	143	94.1	89.1	97.3	54.4	41.6	71.3	<10.0	2560.0
		18-35M	PRE	142	65	45.8	37.4	54.3	21.4	15.9	28.8	<10.0	1280.0
			POST	141	136	96.5	91.9	98.8	207.5	158.3	272.1	<10.0	3620.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	6-17M	PRE	157	29	18.5	12.7	25.4	7.5	6.4	8.7	<10.0	320.0
			POST	152	150	98.7	95.3	99.8	92.8	77.8	110.6	<10.0	905.0
		18-35M	PRE	142	38	26.8	19.7	34.8	8.1	6.9	9.5	<10.0	226.0
			POST	134	132	98.5	94.7	99.8	143.1	117.9	173.8	<10.0	1810.0
	D-TIV-YB	6-17M	PRE	160	28	17.5	12.0	24.3	6.7	5.9	7.6	<10.0	905.0
			POST	152	147	96.7	92.5	98.9	72.3	59.6	87.8	<10.0	1810.0
		18-35M	PRE	142	32	22.5	16.0	30.3	7.8	6.6	9.1	<10.0	226.0
			POST	141	139	98.6	95.0	99.8	166.0	135.3	203.7	<10.0	2560.0
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	6-17M	PRE	157	25	15.9	10.6	22.6	6.8	5.9	7.8	<10.0	453.0
			POST	152	144	94.7	89.9	97.7	66.0	52.6	82.8	<10.0	2560.0
		18-35M	PRE	142	67	47.2	38.8	55.7	17.4	13.5	22.4	<10.0	640.0
			POST	134	133	99.3	95.9	100	200.3	149.7	267.9	<10.0	5120.0
	D-TIV-YB	6-17M	PRE	160	13	8.1	4.4	13.5	5.5	5.2	5.9	<10.0	226.0
			POST	152	55	36.2	28.6	44.4	8.5	7.4	9.8	<10.0	320.0
		18-35M	PRE	142	63	44.4	36.0	52.9	16.7	12.9	21.6	<10.0	905.0
			POST	141	102	72.3	64.2	79.5	30.5	23.3	39.9	<10.0	1280.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 76 Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	6-17M	PRE	157	11	7.0	3.5	12.2
			POST	152	126	82.9	76.0	88.5
		18-35M	PRE	142	38	26.8	19.7	34.8
			POST	134	130	97.0	92.5	99.2
	D-TIV-YB	6-17M	PRE	160	13	8.1	4.4	13.5
			POST	152	62	40.8	32.9	49.0
		18-35M	PRE	142	36	25.4	18.4	33.3
			POST	141	113	80.1	72.6	86.4
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	6-17M	PRE	157	38	24.2	17.7	31.7
			POST	152	115	75.7	68.0	82.2
		18-35M	PRE	142	59	41.5	33.3	50.1
			POST	134	117	87.3	80.5	92.4
	D-TIV-YB	6-17M	PRE	160	24	15.0	9.9	21.5
			POST	152	77	50.7	42.4	58.9
		18-35M	PRE	142	53	37.3	29.4	45.8
			POST	141	119	84.4	77.3	90.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	6-17M	PRE	157	13	8.3	4.5	13.7
			POST	152	124	81.6	74.5	87.4
		18-35M	PRE	142	14	9.9	5.5	16.0
			POST	134	120	89.6	83.1	94.2
	D-TIV-YB	6-17M	PRE	160	10	6.3	3.0	11.2
			POST	152	110	72.4	64.5	79.3
		18-35M	PRE	142	14	9.9	5.5	16.0
			POST	141	125	88.7	82.2	93.4
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	6-17M	PRE	157	10	6.4	3.1	11.4
			POST	152	103	67.8	59.7	75.1
		18-35M	PRE	142	49	34.5	26.7	42.9
			POST	134	114	85.1	77.9	90.6
	D-TIV-YB	6-17M	PRE	160	2	1.3	0.2	4.4
			POST	152	13	8.6	4.6	14.2
		18-35M	PRE	142	46	32.4	24.8	40.8
			POST	141	63	44.7	36.3	53.3

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
SPR = seroprotection rate
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 77 Mean geometric increase (MGI) for HI antibodies against Flu A/CAL/7/09, Flu A/Victoria/361/11, Flu B/Bri/60/08 and Flu B/Hubei-Wujiagang/158/09 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

				MGI		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09 (H1N1). HA Ab (1/DIL)	Q-QIV	6-17M	152	14.7	12.0	18.0
		18-35M	134	18.4	15.5	21.7
	D-TIV-YB	6-17M	152	4.2	3.4	5.2
		18-35M	141	9.8	7.9	12.1
Flu A/Victoria/361/11 (H3N2). HA Ab (1/DIL)	Q-QIV	6-17M	152	8.7	7.2	10.4
		18-35M	134	9.7	7.9	11.9
	D-TIV-YB	6-17M	152	5.9	4.8	7.1
		18-35M	141	9.6	7.7	12.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab (1/DIL)	Q-QIV	6-17M	152	12.4	10.1	15.2
		18-35M	134	17.9	14.6	22.0
	D-TIV-YB	6-17M	152	10.6	8.8	12.8
		18-35M	141	21.6	17.6	26.6
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Q-QIV	6-17M	152	9.6	7.9	11.7
		18-35M	134	11.5	9.9	13.4
	D-TIV-YB	6-17M	152	1.5	1.3	1.8
		18-35M	141	1.9	1.6	2.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = Number of subjects with pre- and post-vaccination results available
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 78 Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	6-17M	152	123	80.9	73.8	86.8
		18-35M	134	123	91.8	85.8	95.8
	D-TIV-YB	6-17M	152	60	39.5	31.6	47.7
		18-35M	141	99	70.2	61.9	77.6
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	6-17M	152	109	71.7	63.8	78.7
		18-35M	134	97	72.4	64.0	79.8
	D-TIV-YB	6-17M	152	65	42.8	34.8	51.0
		18-35M	141	98	69.5	61.2	77.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	6-17M	152	113	74.3	66.6	81.1
		18-35M	134	113	84.3	77.0	90.0
	D-TIV-YB	6-17M	152	105	69.1	61.1	76.3
		18-35M	141	123	87.2	80.6	92.3
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	6-17M	152	101	66.4	58.3	73.9
		18-35M	134	110	82.1	74.5	88.2
	D-TIV-YB	6-17M	152	11	7.2	3.7	12.6
		18-35M	141	18	12.8	7.7	19.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 79 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

				Adjusted GMT ratio (Q-QIV/6-17M / D-TIV-YB/6-17M)		
Q-QIV/6-17M		D-TIV-YB/6-17M			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
152	60.8	152	9.3	6.56	5.15	8.35

D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 80 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

				Adjusted GMT ratio (Q-QIV/18-35M / D-TIV-YB/18-35M)		
Q-QIV/18-35M		D-TIV-YB/18-35M			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
134	194.9	141	31.3	6.23	5.02	7.73

D-TIV-YB = *Fluarix* Vaccine
18-35M = 18-35 months old subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 81 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

								Difference in SCR (Q-QIV/6-17M minus D-TIV-YB/6-17M)		
		Q-QIV/6-17M			D-TIV-YB/6-17M				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	152	101	66.4	152	11	7.2	59.21	50.09	67.19

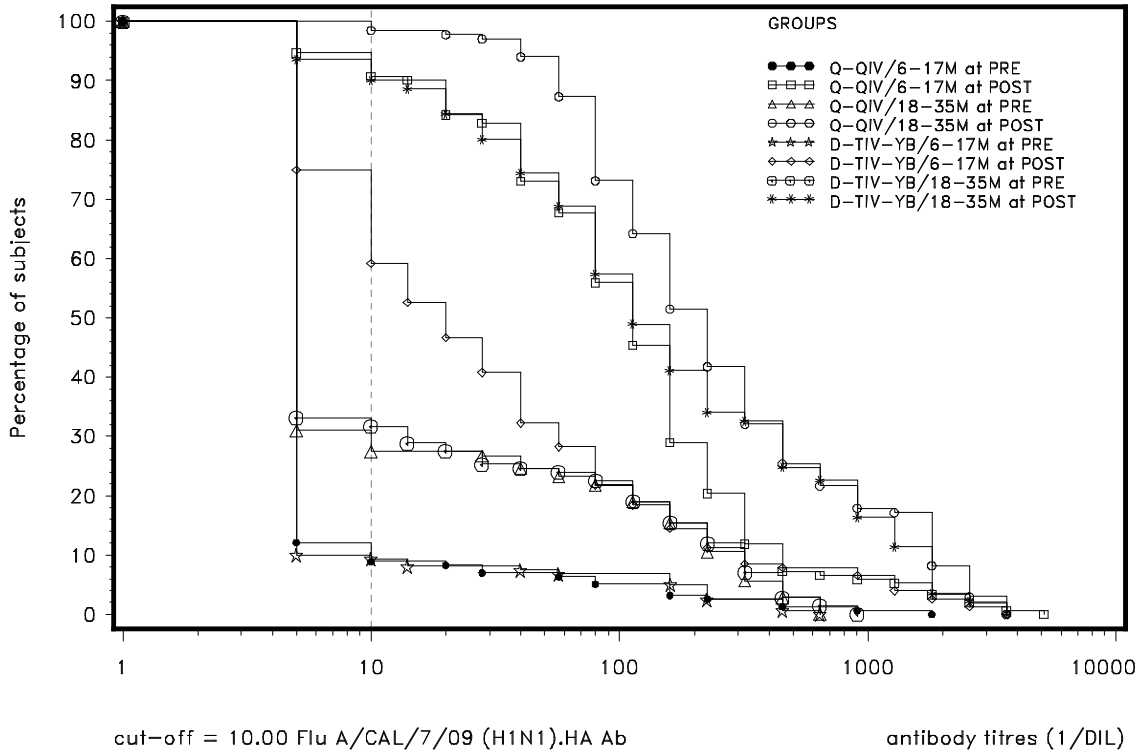
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 82 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By age strata - Total Vaccinated cohort)

								Difference in SCR (Q-QIV/18-35M minus D-TIV-YB/18-35M)		
		Q-QIV/18-35M			D-TIV-YB/18-35M				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	134	110	82.1	141	18	12.8	69.32	59.85	76.90

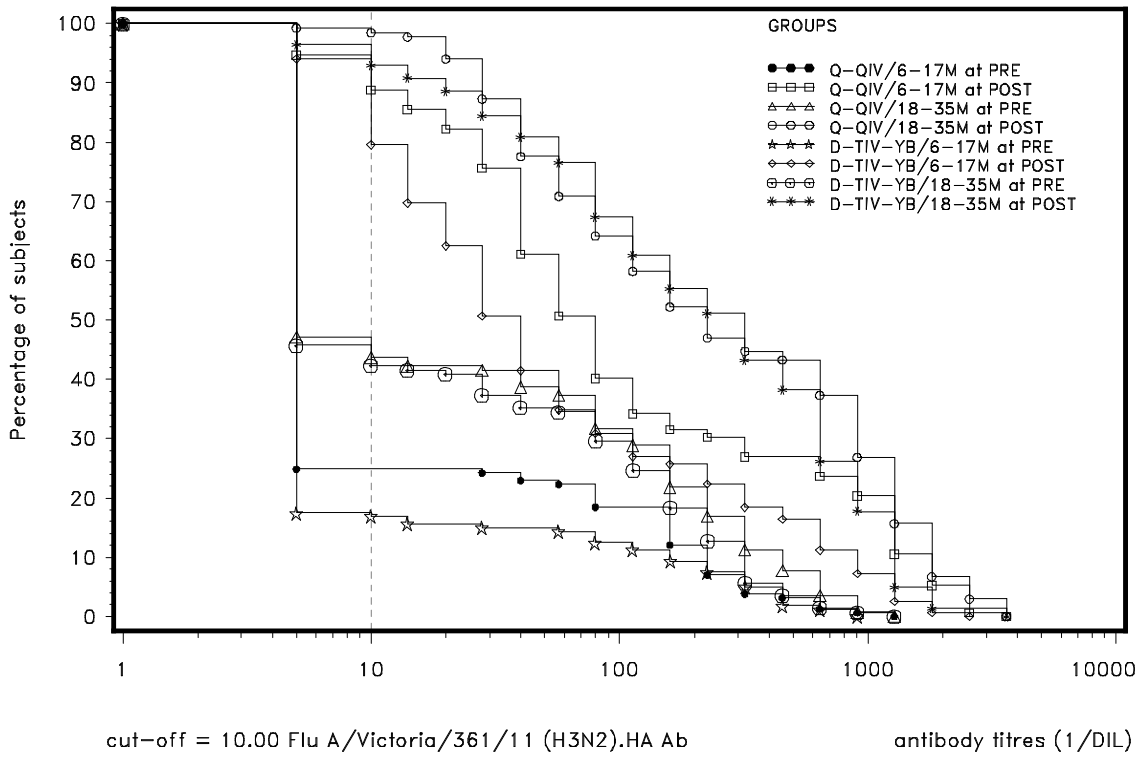
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
18-35M = 18-35 months old subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Figure 18 Reverse cumulative distribution curves for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - Total Vaccinated cohort)



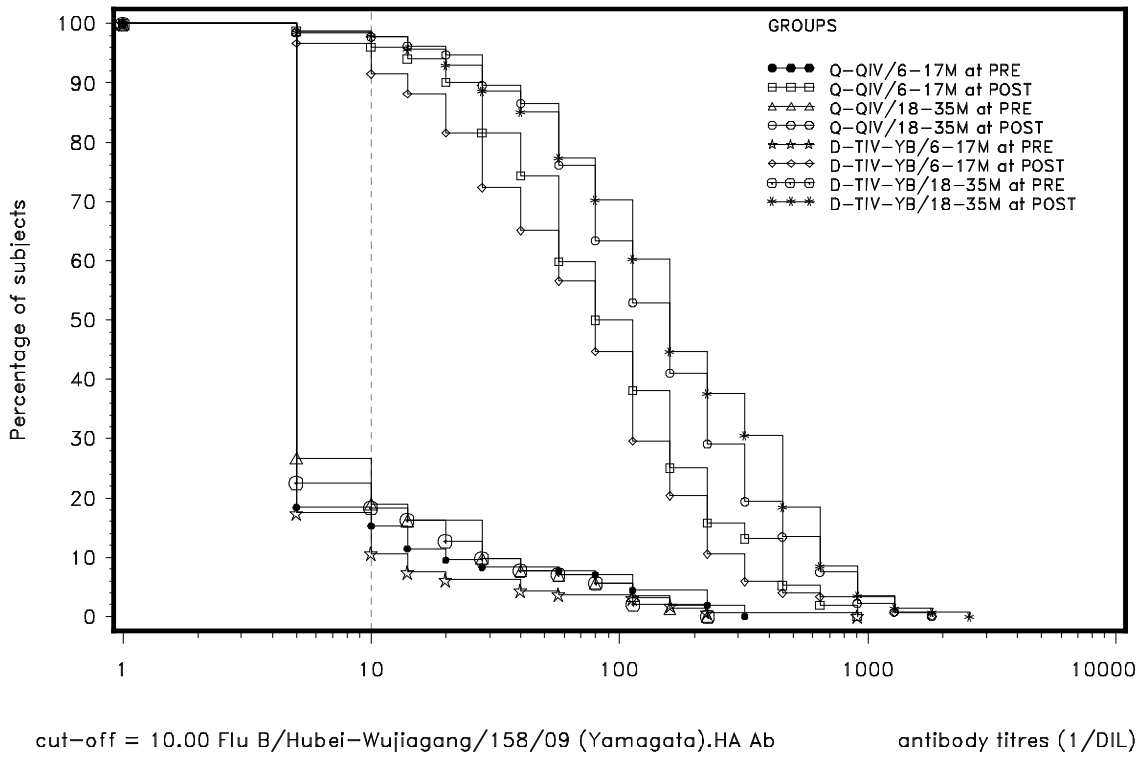
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 19 Reverse cumulative distribution curves for HI antibodies against Flu A/Victoria/361/11 (H3N2). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - Total Vaccinated cohort)



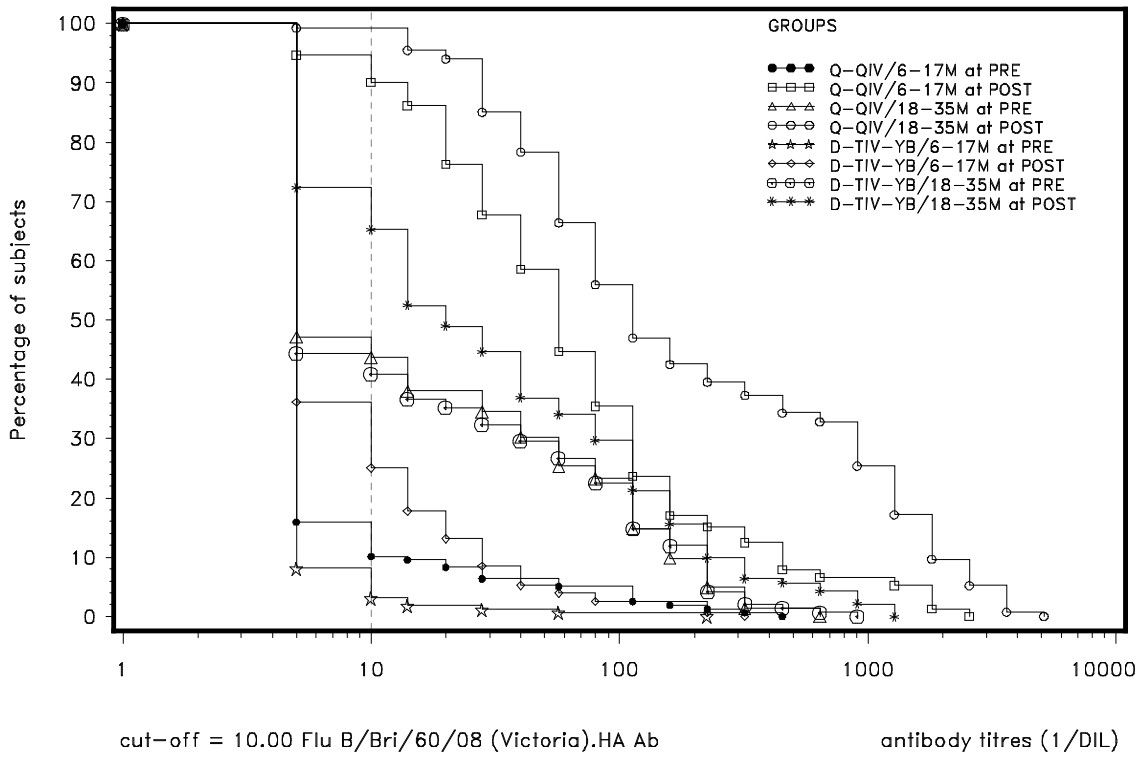
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 20 Reverse cumulative distribution curves for HI antibodies against Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - Totalvaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 21 Reverse cumulative distribution curves for HI antibodies against Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after the last vaccination (By age strata - Total Vaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

10.2.2.3. By priming status

Table 83 Seropositivity rates and GMTs for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

					≥ 10 1/DIL				GMT				
							95% CI			95% CI			
Strain	Group	Sub-group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	UNPRIM	PRE	286	57	19.9	15.5	25.0	9.7	8.2	11.4	<10.0	1810.0
			POST	273	265	97.1	94.3	98.7	161.4	135.9	191.8	<10.0	5120.0
		PRIM	PRE	13	6	46.2	19.2	74.9	8.8	5.3	14.4	<10.0	57.0
			POST	13	13	100	75.3	100	73.9	39.1	139.4	10.0	453.0
	D-TIV-YB	UNPRIM	PRE	287	59	20.6	16.0	25.7	9.8	8.3	11.6	<10.0	905.0
			POST	278	232	83.5	78.6	87.6	62.7	50.1	78.4	<10.0	3620.0
		PRIM	PRE	15	4	26.7	7.8	55.1	9.1	4.2	19.6	<10.0	905.0
			POST	15	14	93.3	68.1	99.8	78.1	27.0	225.9	<10.0	3620.0
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	UNPRIM	PRE	286	105	36.7	31.1	42.6	17.9	14.5	22.1	<10.0	1280.0
			POST	273	264	96.7	93.8	98.5	166.4	134.4	206.0	<10.0	3620.0
		PRIM	PRE	13	1	7.7	0.2	36.0	6.9	3.4	13.8	<10.0	320.0
			POST	13	13	100	75.3	100	53.6	26.3	109.1	10.0	1280.0
	D-TIV-YB	UNPRIM	PRE	287	90	31.4	26.0	37.1	14.1	11.6	17.2	<10.0	1280.0
			POST	278	267	96.0	93.0	98.0	108.6	88.0	134.0	<10.0	3620.0
		PRIM	PRE	15	3	20.0	4.3	48.1	7.4	4.1	13.5	<10.0	320.0
			POST	15	12	80.0	51.9	95.7	43.8	17.5	109.9	<10.0	640.0
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	UNPRIM	PRE	286	64	22.4	17.7	27.7	7.9	7.0	8.8	<10.0	320.0
			POST	273	271	99.3	97.4	99.9	121.2	106.3	138.1	<10.0	1810.0
		PRIM	PRE	13	3	23.1	5.0	53.8	6.0	4.8	7.5	<10.0	14.0
			POST	13	11	84.6	54.6	98.1	29.8	14.9	59.7	<10.0	160.0
	D-TIV-YB	UNPRIM	PRE	287	56	19.5	15.1	24.6	7.2	6.5	8.0	<10.0	905.0
			POST	278	272	97.8	95.4	99.2	113.9	98.2	132.2	<10.0	2560.0
		PRIM	PRE	15	4	26.7	7.8	55.1	7.1	4.8	10.4	<10.0	57.0
			POST	15	14	93.3	68.1	99.8	38.9	17.4	87.0	<10.0	1280.0
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	UNPRIM	PRE	286	83	29.0	23.8	34.7	10.6	9.0	12.3	<10.0	640.0
			POST	273	264	96.7	93.8	98.5	112.1	91.8	136.9	<10.0	5120.0
		PRIM	PRE	13	9	69.2	38.6	90.9	12.3	7.6	20.1	<10.0	57.0
			POST	13	13	100	75.3	100	91.3	52.5	158.6	28.0	640.0
	D-TIV-YB	UNPRIM	PRE	287	65	22.6	17.9	27.9	8.9	7.7	10.2	<10.0	905.0
			POST	278	144	51.8	45.8	57.8	14.8	12.5	17.5	<10.0	1280.0
		PRIM	PRE	15	11	73.3	44.9	92.2	21.9	10.3	46.5	<10.0	320.0
			POST	15	13	86.7	59.5	98.3	48.0	22.2	103.9	<10.0	905.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 84 Seroprotection rates (SPR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

					SPR			
							95% CI	
Strain	Group	Sub-group	Timing	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	UNPRIM	PRE	286	47	16.4	12.3	21.2
			POST	273	246	90.1	85.9	93.4
		PRIM	PRE	13	2	15.4	1.9	45.4
			POST	13	10	76.9	46.2	95.0
	D-TIV-YB	UNPRIM	PRE	287	48	16.7	12.6	21.6
			POST	278	167	60.1	54.1	65.9
		PRIM	PRE	15	1	6.7	0.2	31.9
			POST	15	8	53.3	26.6	78.7
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	UNPRIM	PRE	286	96	33.6	28.1	39.4
			POST	273	223	81.7	76.6	86.1
		PRIM	PRE	13	1	7.7	0.2	36.0
			POST	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	PRE	287	76	26.5	21.5	32.0
			POST	278	188	67.6	61.8	73.1
		PRIM	PRE	15	1	6.7	0.2	31.9
			POST	15	8	53.3	26.6	78.7
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	UNPRIM	PRE	286	27	9.4	6.3	13.4
			POST	273	238	87.2	82.6	90.9
		PRIM	PRE	13	0	0.0	0.0	24.7
			POST	13	6	46.2	19.2	74.9
	D-TIV-YB	UNPRIM	PRE	287	23	8.0	5.1	11.8
			POST	278	230	82.7	77.8	87.0
		PRIM	PRE	15	1	6.7	0.2	31.9
			POST	15	5	33.3	11.8	61.6
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	UNPRIM	PRE	286	57	19.9	15.5	25.0
			POST	273	207	75.8	70.3	80.8
		PRIM	PRE	13	2	15.4	1.9	45.4
			POST	13	10	76.9	46.2	95.0
	D-TIV-YB	UNPRIM	PRE	287	44	15.3	11.4	20.0
			POST	278	67	24.1	19.2	29.6
		PRIM	PRE	15	4	26.7	7.8	55.1
			POST	15	9	60.0	32.3	83.7

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = Number of subjects with available results
n/% = Number/percentage of seroprotected subjects (HI titre ≥ 40 1/DIL)
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
SPR = seroprotection rate
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Table 85 Mean geometric increase (MGI) for HI antibodies against Flu A/CAL/7/09, Flu A/Victoria/361/11, Flu B/Bri/60/08 and Flu B/Hubei-Wujiagang/158/09 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

				MGI		
					95% CI	
Strain	**Group**	**Sub-group**	**N**	**Value**	**LL**	**UL**
Flu A/CAL/7/09 (H1N1). HA Ab (1/DIL)	Q-QIV	UNPRIM	273	16.8	14.7	19.3
		PRIM	13	8.4	5.4	13.1
	D-TIV-YB	UNPRIM	278	6.2	5.3	7.3
		PRIM	15	8.6	3.7	20.0
Flu A/Victoria/361/11 (H3N2). HA Ab (1/DIL)	Q-QIV	UNPRIM	273	9.2	8.0	10.6
		PRIM	13	7.8	5.0	12.0
	D-TIV-YB	UNPRIM	278	7.5	6.5	8.8
		PRIM	15	5.9	2.7	12.9
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab (1/DIL)	Q-QIV	UNPRIM	273	15.5	13.4	18.0
		PRIM	13	4.9	2.7	8.9
	D-TIV-YB	UNPRIM	278	15.8	13.6	18.3
		PRIM	15	5.5	3.3	9.3
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Q-QIV	UNPRIM	273	10.6	9.3	12.1
		PRIM	13	7.4	4.8	11.5
	D-TIV-YB	UNPRIM	278	1.7	1.5	1.9
		PRIM	15	2.2	1.4	3.5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = Number of subjects with pre- and post-vaccination results available
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 86 Seroconversion rate (SCR) for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab, Flu A/Victoria/361/11 (H3N2). HA Ab, Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab and Flu B/Bri/60/08 (Victoria). HA Ab 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

				SCR			
						95% CI	
Strain	Group	Sub-group	N	n	%	LL	UL
Flu A/CAL/7/09 (H1N1). HA Ab	Q-QIV	UNPRIM	273	237	86.8	82.2	90.6
		PRIM	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	278	152	54.7	48.6	60.6
		PRIM	15	7	46.7	21.3	73.4
Flu A/Victoria/361/11 (H3N2). HA Ab	Q-QIV	UNPRIM	273	197	72.2	66.4	77.4
		PRIM	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	278	156	56.1	50.1	62.0
		PRIM	15	7	46.7	21.3	73.4
Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab	Q-QIV	UNPRIM	273	220	80.6	75.4	85.1
		PRIM	13	6	46.2	19.2	74.9
	D-TIV-YB	UNPRIM	278	223	80.2	75.0	84.7
		PRIM	15	5	33.3	11.8	61.6
Flu B/Bri/60/08 (Victoria). HA Ab	Q-QIV	UNPRIM	273	202	74.0	68.4	79.1
		PRIM	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	278	27	9.7	6.5	13.8
		PRIM	15	2	13.3	1.7	40.5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = Number of subjects with pre- and post-vaccination results available
n/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 87 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

				Adjusted GMT ratio (Q-QIV/UNPRIM / D-TIV-YB/UNPRIM)		
Q-QIV/UNPRIM		D-TIV-YB/UNPRIM			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
273	103.7	278	16.0	6.47	5.47	7.67

D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 88 Adjusted GMT ratios of antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

				Adjusted GMT ratio (Q-QIV/PRIM / D-TIV-YB/PRIM)		
Q-QIV/PRIM		D-TIV-YB/PRIM			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
13	116.8	15	38.8	3.01	1.61	5.65

D-TIV-YB = *Fluarix* Vaccine; PRIM = Primed subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 89 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

								Difference in SCR (Q-QIV/UNPRIM minus D-TIV-YB/UNPRIM)		
		Q-QIV/UNPRIM			D-TIV-YB/UNPRIM				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	273	202	74.0	278	27	9.7	64.28	57.62	70.13

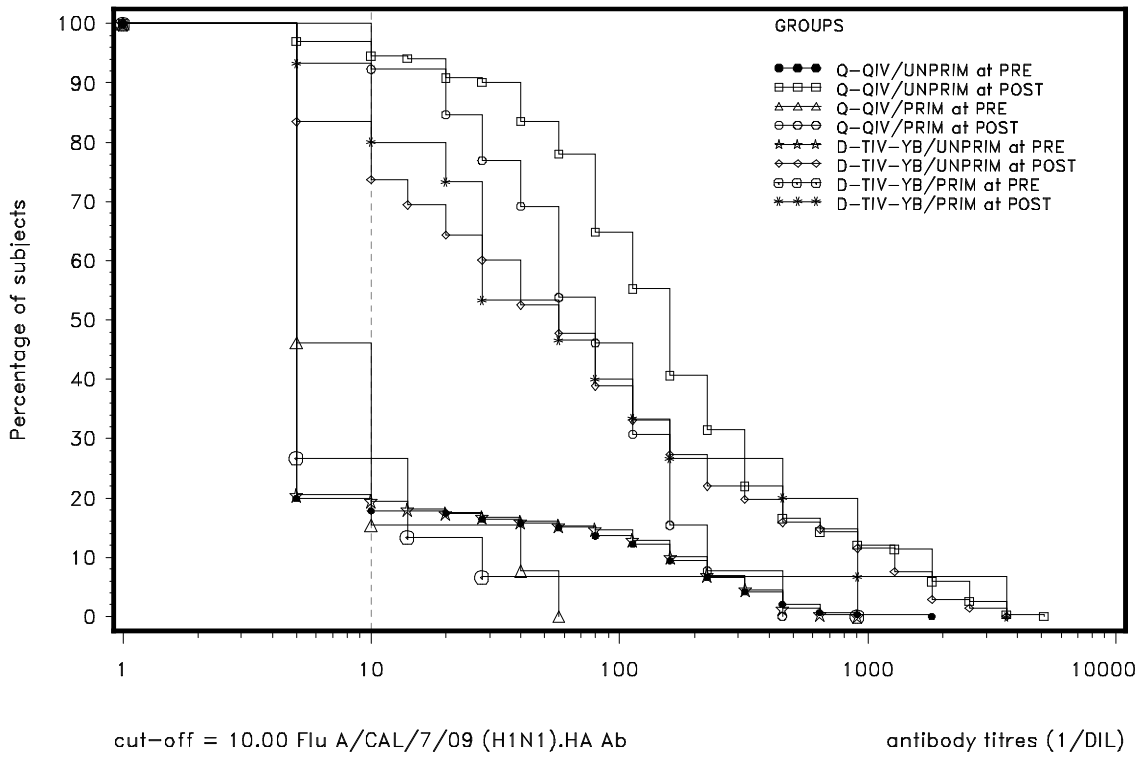
Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine; UNPRIM = Unprimed subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of subjects with a vaccine response
95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 90 Difference in SCR of HI antibody between FLU Q-QIV and D-TIV-YB for the Flu B/Bri/60/08 (Victoria). HA Ab strain 28 days after last vaccine dose (By priming status - Total Vaccinated cohort)

								Difference in SCR (Q-QIV/PRIM minus D-TIV-YB/PRIM)		
		Q-QIV/PRIM			D-TIV-YB/PRIM				95% CI	
Antibody	Pre-vaccination status	N	n	%	N	n	%	%	LL	UL
Flu B/Bri/60/08 (Victoria). HA Ab (1/DIL)	Total	13	9	69.2	15	2	13.3	55.90	19.80	79.11

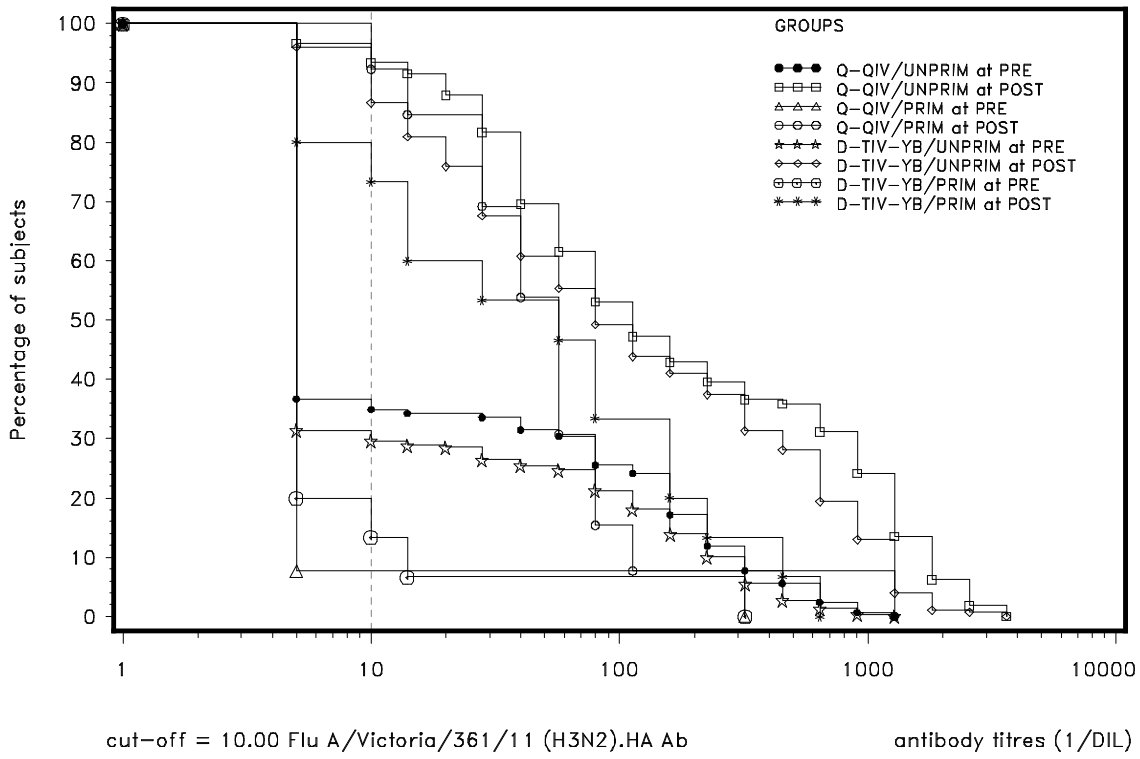
Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine; PRIM = Primed subjects
SCR defined as :
For initially seronegative subjects : post-vaccination antibody titre ≥ 40 1/DIL at POST
For initially seropositive subjects : antibody titre at POST ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available; n/% = number/percentage of subjects with a vaccine response; 95% CI = Standardised asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Figure 22 Reverse cumulative distribution curves for HI antibodies against Flu A/CAL/7/09 (H1N1). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - Total Vaccinated cohort)



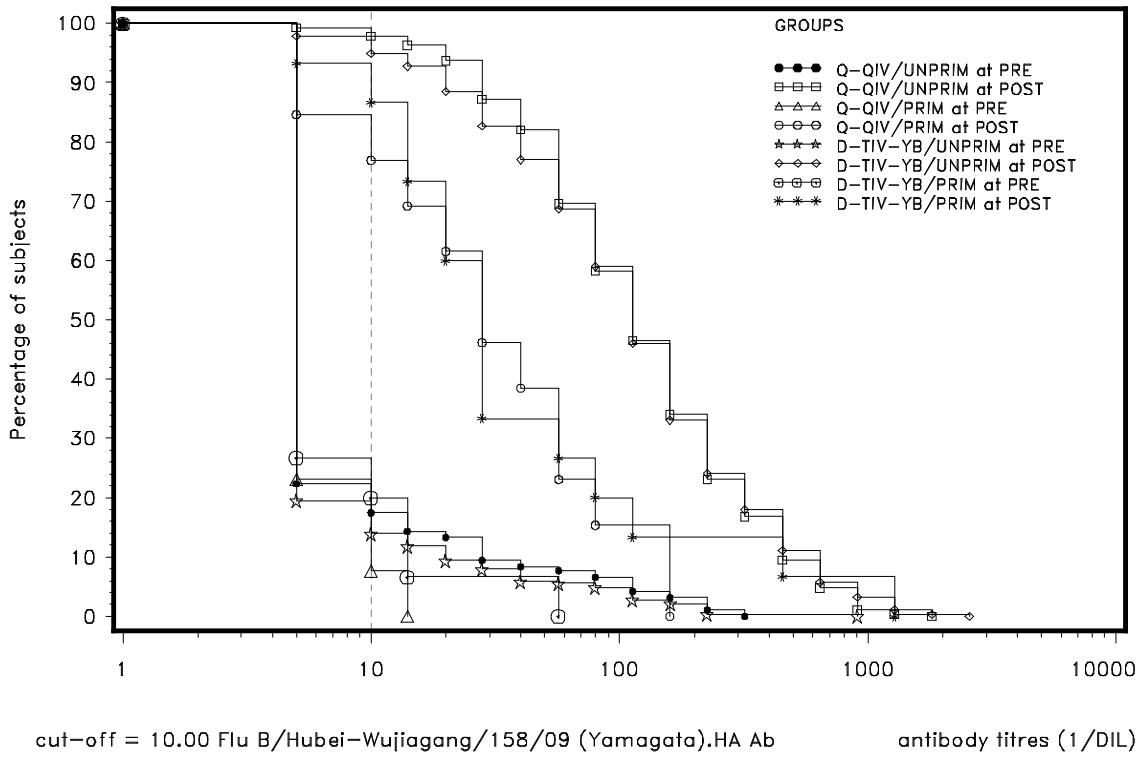
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 23 Reverse cumulative distribution curves for HI antibodies against Flu A/Victoria/361/11 (H3N2). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - Total Vaccinated cohort)



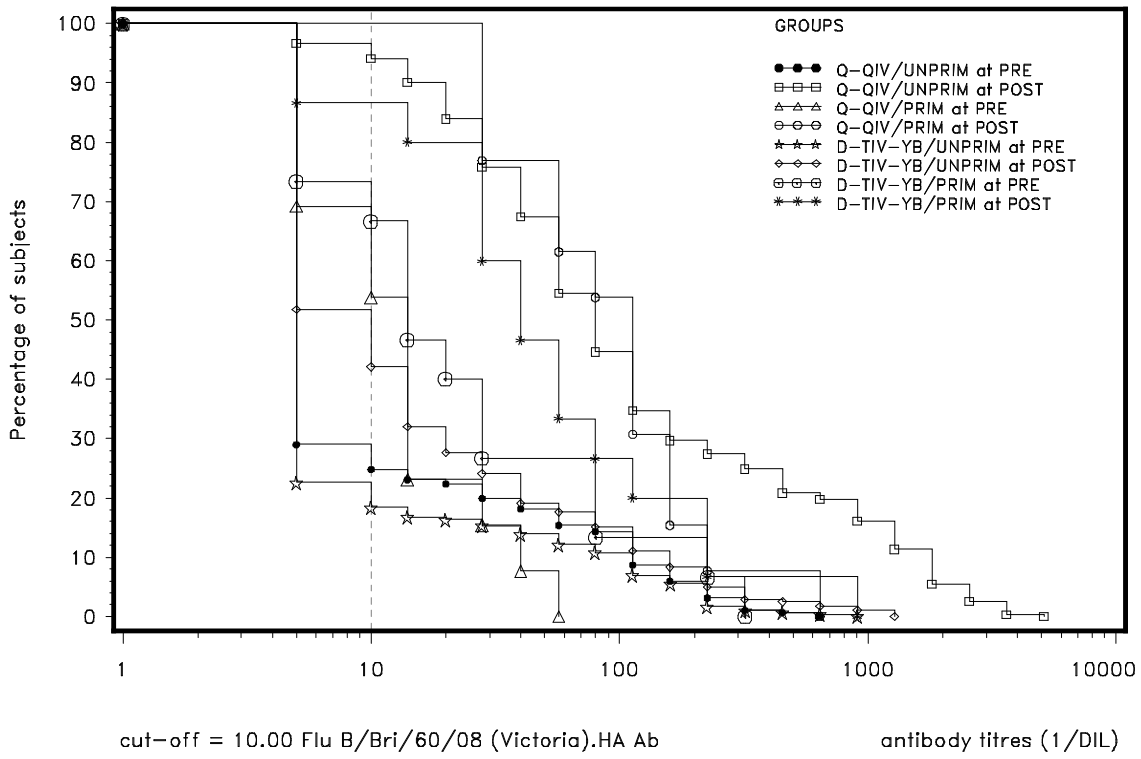
Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 24 Reverse cumulative distribution curves for HI antibodies against Flu B/Hubei-Wujiagang/158/09 (Yamagata). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - Totalvaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

Figure 25 Reverse cumulative distribution curves for HI antibodies against Flu B/Bri/60/08 (Victoria). HA Ab at Day 0 and 28 days after the last vaccination (By priming status - Total Vaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
PRE = Pre-vaccination at Visit Day 0
POST = Post-Vaccination (Visit Day 28 [for primed subjects] and Visit Day 56 [for unprimed subjects])

10.3. Reactogenicity and safety results

10.3.1. Overall

Table 91 Number and percentage of subjects who received study vaccine dose(s) (Total Vaccinated cohort)

	Q-QIV N = 299		D-TIV-YB N = 302	
Total number of doses received	**n**	**%**	**n**	**%**
1	22	7.4	21	7.0
2	277	92.6	281	93.0
Any	299	100	302	100

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
N = number of subjects in each group included in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose

Table 92 Compliance in returning symptom sheets (Total Vaccinated cohort)

Dose	Group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
1	Q-QIV	299	6	289	96.7	290	97.0
	D-TIV-YB	302	8	296	98.0	297	98.3
2	Q-QIV	277	0	272	98.2	274	98.9
	D-TIV-YB	281	2	276	98.2	276	98.2
Total	Q-QIV	576	6	561	97.4	564	97.9
	D-TIV-YB	583	10	572	98.1	573	98.3

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
SS = Symptom sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom sheet return / number of administered doses) X 100

Table 93 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	299	159	53.2	47.3	58.9	299	149	49.8	44.0	55.6	299	77	25.8	20.9	31.1
	D-TIV-YB	302	169	56.0	50.2	61.6	302	152	50.3	44.5	56.1	302	68	22.5	17.9	27.7
Dose 2	Q-QIV	277	126	45.5	39.5	51.6	277	112	40.4	34.6	46.5	277	58	20.9	16.3	26.2
	D-TIV-YB	281	133	47.3	41.4	53.3	281	118	42.0	36.2	48.0	281	63	22.4	17.7	27.8
Overall/dose	Q-QIV	576	285	49.5	45.3	53.6	576	261	45.3	41.2	49.5	576	135	23.4	20.0	27.1
	D-TIV-YB	583	302	51.8	47.7	55.9	583	270	46.3	42.2	50.5	583	131	22.5	19.1	26.1
Overall/subject	Q-QIV	299	190	63.5	57.8	69.0	299	179	59.9	54.1	65.5	299	98	32.8	27.5	38.4
	D-TIV-YB	302	205	67.9	62.3	73.1	302	189	62.6	56.9	68.1	302	96	31.8	26.6	37.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 94 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	299	31	10.4	7.2	14.4	299	30	10.0	6.9	14.0	299	5	1.7	0.5	3.9
	D-TIV-YB	302	22	7.3	4.6	10.8	302	22	7.3	4.6	10.8	302	1	0.3	0.0	1.8
Dose 2	Q-QIV	277	24	8.7	5.6	12.6	277	23	8.3	5.3	12.2	277	3	1.1	0.2	3.1
	D-TIV-YB	281	18	6.4	3.8	9.9	281	16	5.7	3.3	9.1	281	3	1.1	0.2	3.1
Overall/dose	Q-QIV	576	55	9.5	7.3	12.2	576	53	9.2	7.0	11.9	576	8	1.4	0.6	2.7
	D-TIV-YB	583	40	6.9	4.9	9.2	583	38	6.5	4.7	8.8	583	4	0.7	0.2	1.7
Overall/subject	Q-QIV	299	47	15.7	11.8	20.3	299	46	15.4	11.5	20.0	299	7	2.3	0.9	4.8
	D-TIV-YB	302	36	11.9	8.5	16.1	302	35	11.6	8.2	15.7	302	3	1.0	0.2	2.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 95 Incidence and nature of symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	299	143	47.8	42.0	53.7	299	124	41.5	35.8	47.3	299	77	25.8	20.9	31.1
	D-TIV-YB	302	141	46.7	41.0	52.5	302	115	38.1	32.6	43.8	302	67	22.2	17.6	27.3
Dose 2	Q-QIV	277	110	39.7	33.9	45.7	277	89	32.1	26.7	38.0	277	58	20.9	16.3	26.2
	D-TIV-YB	281	115	40.9	35.1	46.9	281	95	33.8	28.3	39.7	281	62	22.1	17.4	27.4
Overall/dose	Q-QIV	576	253	43.9	39.8	48.1	576	213	37.0	33.0	41.1	576	135	23.4	20.0	27.1
	D-TIV-YB	583	256	43.9	39.8	48.0	583	210	36.0	32.1	40.1	583	129	22.1	18.8	25.7
Overall/subject	Q-QIV	299	170	56.9	51.0	62.5	299	148	49.5	43.7	55.3	299	98	32.8	27.5	38.4
	D-TIV-YB	302	175	57.9	52.2	63.6	302	152	50.3	44.5	56.1	302	94	31.1	25.9	36.7

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 96 Incidence and nature of grade 3 symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	299	24	8.0	5.2	11.7	299	23	7.7	4.9	11.3	299	5	1.7	0.5	3.9
	D-TIV-YB	302	15	5.0	2.8	8.1	302	15	5.0	2.8	8.1	302	1	0.3	0.0	1.8
Dose 2	Q-QIV	277	18	6.5	3.9	10.1	277	17	6.1	3.6	9.6	277	3	1.1	0.2	3.1
	D-TIV-YB	281	16	5.7	3.3	9.1	281	14	5.0	2.8	8.2	281	3	1.1	0.2	3.1
Overall/dose	Q-QIV	576	42	7.3	5.3	9.7	576	40	6.9	5.0	9.3	576	8	1.4	0.6	2.7
	D-TIV-YB	583	31	5.3	3.6	7.5	583	29	5.0	3.4	7.1	583	4	0.7	0.2	1.7
Overall/subject	Q-QIV	299	37	12.4	8.9	16.7	299	36	12.0	8.6	16.3	299	7	2.3	0.9	4.8
	D-TIV-YB	302	28	9.3	6.2	13.1	302	27	8.9	6.0	12.7	302	3	1.0	0.2	2.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 97 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

		Q-QIV					D-TIV-YB					Total				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Pain	All	290	73	25.2	20.3	30.6	297	64	21.5	17.0	26.7	587	137	23.3	20.0	27.0
	Grade 2 or 3	290	16	5.5	3.2	8.8	297	7	2.4	1.0	4.8	587	23	3.9	2.5	5.8
	Grade 3	290	5	1.7	0.6	4.0	297	1	0.3	0.0	1.9	587	6	1.0	0.4	2.2
	Medical advice	290	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	587	0	0.0	0.0	0.6
Redness (mm)	All	290	3	1.0	0.2	3.0	297	2	0.7	0.1	2.4	587	5	0.9	0.3	2.0
	>50.0	290	1	0.3	0.0	1.9	297	0	0.0	0.0	1.2	587	1	0.2	0.0	0.9
	>100	290	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	587	0	0.0	0.0	0.6
	Medical advice	290	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	587	0	0.0	0.0	0.6
Swelling (mm)	All	290	2	0.7	0.1	2.5	297	2	0.7	0.1	2.4	587	4	0.7	0.2	1.7
	>50.0	290	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	587	0	0.0	0.0	0.6
	>100	290	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	587	0	0.0	0.0	0.6
	Medical advice	290	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	587	0	0.0	0.0	0.6
Dose 2																
Pain	All	274	57	20.8	16.2	26.1	276	59	21.4	16.7	26.7	550	116	21.1	17.8	24.7
	Grade 2 or 3	274	18	6.6	3.9	10.2	276	15	5.4	3.1	8.8	550	33	6.0	4.2	8.3
	Grade 3	274	3	1.1	0.2	3.2	276	3	1.1	0.2	3.1	550	6	1.1	0.4	2.4
	Medical advice	274	1	0.4	0.0	2.0	276	0	0.0	0.0	1.3	550	1	0.2	0.0	1.0
Redness (mm)	All	274	4	1.5	0.4	3.7	276	4	1.4	0.4	3.7	550	8	1.5	0.6	2.8
	>50.0	274	1	0.4	0.0	2.0	276	0	0.0	0.0	1.3	550	1	0.2	0.0	1.0
	>100	274	0	0.0	0.0	1.3	276	0	0.0	0.0	1.3	550	0	0.0	0.0	0.7
	Medical advice	274	1	0.4	0.0	2.0	276	0	0.0	0.0	1.3	550	1	0.2	0.0	1.0
Swelling (mm)	All	274	4	1.5	0.4	3.7	276	5	1.8	0.6	4.2	550	9	1.6	0.8	3.1
	>50.0	274	1	0.4	0.0	2.0	276	0	0.0	0.0	1.3	550	1	0.2	0.0	1.0
	>100	274	0	0.0	0.0	1.3	276	0	0.0	0.0	1.3	550	0	0.0	0.0	0.7
	Medical advice	274	1	0.4	0.0	2.0	276	0	0.0	0.0	1.3	550	1	0.2	0.0	1.0
Overall/dose																
Pain	All	564	130	23.0	19.6	26.8	573	123	21.5	18.2	25.1	1137	253	22.3	19.9	24.8
	Grade 2 or 3	564	34	6.0	4.2	8.3	573	22	3.8	2.4	5.8	1137	56	4.9	3.7	6.3
	Grade 3	564	8	1.4	0.6	2.8	573	4	0.7	0.2	1.8	1137	12	1.1	0.5	1.8
	Medical advice	564	1	0.2	0.0	1.0	573	0	0.0	0.0	0.6	1137	1	0.1	0.0	0.5
Redness (mm)	All	564	7	1.2	0.5	2.5	573	6	1.0	0.4	2.3	1137	13	1.1	0.6	1.9
	>50.0	564	2	0.4	0.0	1.3	573	0	0.0	0.0	0.6	1137	2	0.2	0.0	0.6
	>100	564	0	0.0	0.0	0.7	573	0	0.0	0.0	0.6	1137	0	0.0	0.0	0.3
	Medical advice	564	1	0.2	0.0	1.0	573	0	0.0	0.0	0.6	1137	1	0.1	0.0	0.5
Swelling (mm)	All	564	6	1.1	0.4	2.3	573	7	1.2	0.5	2.5	1137	13	1.1	0.6	1.9
	>50.0	564	1	0.2	0.0	1.0	573	0	0.0	0.0	0.6	1137	1	0.1	0.0	0.5
	>100	564	0	0.0	0.0	0.7	573	0	0.0	0.0	0.6	1137	0	0.0	0.0	0.3
	Medical advice	564	1	0.2	0.0	1.0	573	0	0.0	0.0	0.6	1137	1	0.1	0.0	0.5
Overall/subject																
Pain	All	291	95	32.6	27.3	38.4	297	91	30.6	25.4	36.2	588	186	31.6	27.9	35.6
	Grade 2 or 3	291	27	9.3	6.2	13.2	297	19	6.4	3.9	9.8	588	46	7.8	5.8	10.3
	Grade 3	291	7	2.4	1.0	4.9	297	3	1.0	0.2	2.9	588	10	1.7	0.8	3.1
	Medical advice	291	1	0.3	0.0	1.9	297	0	0.0	0.0	1.2	588	1	0.2	0.0	0.9
Redness (mm)	All	291	6	2.1	0.8	4.4	297	6	2.0	0.7	4.3	588	12	2.0	1.1	3.5
	>50.0	291	2	0.7	0.1	2.5	297	0	0.0	0.0	1.2	588	2	0.3	0.0	1.2
	>100	291	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	588	0	0.0	0.0	0.6
	Medical advice	291	1	0.3	0.0	1.9	297	0	0.0	0.0	1.2	588	1	0.2	0.0	0.9

		Q-QIV					D-TIV-YB					Total				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Swelling (mm)	All	291	5	1.7	0.6	4.0	297	6	2.0	0.7	4.3	588	11	1.9	0.9	3.3
	>50.0	291	1	0.3	0.0	1.9	297	0	0.0	0.0	1.2	588	1	0.2	0.0	0.9
	>100	291	0	0.0	0.0	1.3	297	0	0.0	0.0	1.2	588	0	0.0	0.0	0.6
	Medical advice	291	1	0.3	0.0	1.9	297	0	0.0	0.0	1.2	588	1	0.2	0.0	0.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
Total : n/%= number/percentage of subjects/doses with at least one local symptom whatever the number of injections.
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 98 Incidence of solicited general symptoms (excluding fever) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

		Q-QIV					D-TIV-YB					Total				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Drowsiness	All	289	72	24.9	20.0	30.3	296	64	21.6	17.1	26.8	585	136	23.2	19.9	26.9
	Grade 2 or 3	289	26	9.0	6.0	12.9	296	18	6.1	3.6	9.4	585	44	7.5	5.5	10.0
	Grade 3	289	6	2.1	0.8	4.5	296	4	1.4	0.4	3.4	585	10	1.7	0.8	3.1
	Related	289	59	20.4	15.9	25.5	296	55	18.6	14.3	23.5	585	114	19.5	16.4	22.9
	Grade 2 or 3 Related	289	21	7.3	4.6	10.9	296	16	5.4	3.1	8.6	585	37	6.3	4.5	8.6
	Grade 3 Related	289	5	1.7	0.6	4.0	296	3	1.0	0.2	2.9	585	8	1.4	0.6	2.7
	Medical advice	289	9	3.1	1.4	5.8	296	2	0.7	0.1	2.4	585	11	1.9	0.9	3.3
Irritability / fussiness	All	289	91	31.5	26.2	37.2	296	94	31.8	26.5	37.4	585	185	31.6	27.9	35.6
	Grade 2 or 3	289	35	12.1	8.6	16.4	296	31	10.5	7.2	14.5	585	66	11.3	8.8	14.1
	Grade 3	289	11	3.8	1.9	6.7	296	10	3.4	1.6	6.1	585	21	3.6	2.2	5.4
	Related	289	80	27.7	22.6	33.2	296	76	25.7	20.8	31.0	585	156	26.7	23.1	30.4
	Grade 2 or 3 Related	289	29	10.0	6.8	14.1	296	24	8.1	5.3	11.8	585	53	9.1	6.9	11.7
	Grade 3 Related	289	9	3.1	1.4	5.8	296	8	2.7	1.2	5.3	585	17	2.9	1.7	4.6
	Medical advice	289	10	3.5	1.7	6.3	296	6	2.0	0.7	4.4	585	16	2.7	1.6	4.4
Loss of appetite	All	289	78	27.0	22.0	32.5	296	71	24.0	19.2	29.3	585	149	25.5	22.0	29.2
	Grade 2 or 3	289	32	11.1	7.7	15.3	296	21	7.1	4.4	10.6	585	53	9.1	6.9	11.7
	Grade 3	289	9	3.1	1.4	5.8	296	7	2.4	1.0	4.8	585	16	2.7	1.6	4.4
	Related	289	67	23.2	18.4	28.5	296	57	19.3	14.9	24.2	585	124	21.2	18.0	24.7
	Grade 2 or 3 Related	289	27	9.3	6.2	13.3	296	15	5.1	2.9	8.2	585	42	7.2	5.2	9.6
	Grade 3 Related	289	9	3.1	1.4	5.8	296	3	1.0	0.2	2.9	585	12	2.1	1.1	3.6
	Medical advice	289	8	2.8	1.2	5.4	296	5	1.7	0.6	3.9	585	13	2.2	1.2	3.8

		Q-QIV					D-TIV-YB					Total				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 2																
Drowsiness	All	272	49	18.0	13.6	23.1	276	44	15.9	11.8	20.8	548	93	17.0	13.9	20.4
	Grade 2 or 3	272	15	5.5	3.1	8.9	276	13	4.7	2.5	7.9	548	28	5.1	3.4	7.3
	Grade 3	272	3	1.1	0.2	3.2	276	5	1.8	0.6	4.2	548	8	1.5	0.6	2.9
	Related	272	42	15.4	11.4	20.3	276	42	15.2	11.2	20.0	548	84	15.3	12.4	18.6
	Grade 2 or 3 Related	272	11	4.0	2.0	7.1	276	12	4.3	2.3	7.5	548	23	4.2	2.7	6.2
	Grade 3 Related	272	2	0.7	0.1	2.6	276	5	1.8	0.6	4.2	548	7	1.3	0.5	2.6
	Medical advice	272	6	2.2	0.8	4.7	276	1	0.4	0.0	2.0	548	7	1.3	0.5	2.6
Irritability / fussiness	All	272	72	26.5	21.3	32.1	276	75	27.2	22.0	32.8	548	147	26.8	23.2	30.7
	Grade 2 or 3	272	26	9.6	6.3	13.7	276	28	10.1	6.8	14.3	548	54	9.9	7.5	12.7
	Grade 3	272	6	2.2	0.8	4.7	276	5	1.8	0.6	4.2	548	11	2.0	1.0	3.6
	Related	272	63	23.2	18.3	28.6	276	67	24.3	19.3	29.8	548	130	23.7	20.2	27.5
	Grade 2 or 3 Related	272	22	8.1	5.1	12.0	276	23	8.3	5.4	12.2	548	45	8.2	6.1	10.8
	Grade 3 Related	272	4	1.5	0.4	3.7	276	4	1.4	0.4	3.7	548	8	1.5	0.6	2.9
	Medical advice	272	6	2.2	0.8	4.7	276	1	0.4	0.0	2.0	548	7	1.3	0.5	2.6
Loss of appetite	All	272	48	17.6	13.3	22.7	276	55	19.9	15.4	25.1	548	103	18.8	15.6	22.3
	Grade 2 or 3	272	20	7.4	4.5	11.1	276	18	6.5	3.9	10.1	548	38	6.9	5.0	9.4
	Grade 3	272	8	2.9	1.3	5.7	276	8	2.9	1.3	5.6	548	16	2.9	1.7	4.7
	Related	272	40	14.7	10.7	19.5	276	46	16.7	12.5	21.6	548	86	15.7	12.7	19.0
	Grade 2 or 3 Related	272	17	6.3	3.7	9.8	276	16	5.8	3.3	9.2	548	33	6.0	4.2	8.4
	Grade 3 Related	272	8	2.9	1.3	5.7	276	8	2.9	1.3	5.6	548	16	2.9	1.7	4.7
	Medical advice	272	8	2.9	1.3	5.7	276	3	1.1	0.2	3.1	548	11	2.0	1.0	3.6
Overall/dose																
Drowsiness	All	561	121	21.6	18.2	25.2	572	108	18.9	15.8	22.3	1133	229	20.2	17.9	22.7
	Grade 2 or 3	561	41	7.3	5.3	9.8	572	31	5.4	3.7	7.6	1133	72	6.4	5.0	7.9
	Grade 3	561	9	1.6	0.7	3.0	572	9	1.6	0.7	3.0	1133	18	1.6	0.9	2.5
	Related	561	101	18.0	14.9	21.4	572	97	17.0	14.0	20.3	1133	198	17.5	15.3	19.8
	Grade 2 or 3 Related	561	32	5.7	3.9	8.0	572	28	4.9	3.3	7.0	1133	60	5.3	4.1	6.8
	Grade 3 Related	561	7	1.2	0.5	2.6	572	8	1.4	0.6	2.7	1133	15	1.3	0.7	2.2
	Medical advice	561	15	2.7	1.5	4.4	572	3	0.5	0.1	1.5	1133	18	1.6	0.9	2.5
Irritability / fussiness	All	561	163	29.1	25.3	33.0	572	169	29.5	25.8	33.5	1133	332	29.3	26.7	32.0
	Grade 2 or 3	561	61	10.9	8.4	13.7	572	59	10.3	7.9	13.1	1133	120	10.6	8.9	12.5
	Grade 3	561	17	3.0	1.8	4.8	572	15	2.6	1.5	4.3	1133	32	2.8	1.9	4.0
	Related	561	143	25.5	21.9	29.3	572	143	25.0	21.5	28.8	1133	286	25.2	22.7	27.9
	Grade 2 or 3 Related	561	51	9.1	6.8	11.8	572	47	8.2	6.1	10.8	1133	98	8.6	7.1	10.4
	Grade 3 Related	561	13	2.3	1.2	3.9	572	12	2.1	1.1	3.6	1133	25	2.2	1.4	3.2
	Medical advice	561	16	2.9	1.6	4.6	572	7	1.2	0.5	2.5	1133	23	2.0	1.3	3.0
Loss of appetite	All	561	126	22.5	19.1	26.1	572	126	22.0	18.7	25.7	1133	252	22.2	19.9	24.8
	Grade 2 or 3	561	52	9.3	7.0	12.0	572	39	6.8	4.9	9.2	1133	91	8.0	6.5	9.8
	Grade 3	561	17	3.0	1.8	4.8	572	15	2.6	1.5	4.3	1133	32	2.8	1.9	4.0
	Related	561	107	19.1	15.9	22.6	572	103	18.0	14.9	21.4	1133	210	18.5	16.3	20.9
	Grade 2 or 3 Related	561	44	7.8	5.8	10.4	572	31	5.4	3.7	7.6	1133	75	6.6	5.2	8.2
	Grade 3 Related	561	17	3.0	1.8	4.8	572	11	1.9	1.0	3.4	1133	28	2.5	1.6	3.6
	Medical advice	561	16	2.9	1.6	4.6	572	8	1.4	0.6	2.7	1133	24	2.1	1.4	3.1

		Q-QIV					D-TIV-YB					Total				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject																
Drowsiness	All	290	93	32.1	26.7	37.8	296	88	29.7	24.6	35.3	586	181	30.9	27.2	34.8
	Grade 2 or 3	290	34	11.7	8.3	16.0	296	27	9.1	6.1	13.0	586	61	10.4	8.1	13.2
	Grade 3	290	9	3.1	1.4	5.8	296	9	3.0	1.4	5.7	586	18	3.1	1.8	4.8
	Related	290	79	27.2	22.2	32.8	296	80	27.0	22.1	32.5	586	159	27.1	23.6	30.9
	Grade 2 or 3 Related	290	28	9.7	6.5	13.7	296	24	8.1	5.3	11.8	586	52	8.9	6.7	11.5
	Grade 3 Related	290	7	2.4	1.0	4.9	296	8	2.7	1.2	5.3	586	15	2.6	1.4	4.2
	Medical advice	290	13	4.5	2.4	7.5	296	3	1.0	0.2	2.9	586	16	2.7	1.6	4.4
Irritability / fussiness	All	290	118	40.7	35.0	46.6	296	123	41.6	35.9	47.4	586	241	41.1	37.1	45.2
	Grade 2 or 3	290	54	18.6	14.3	23.6	296	51	17.2	13.1	22.0	586	105	17.9	14.9	21.3
	Grade 3	290	15	5.2	2.9	8.4	296	14	4.7	2.6	7.8	586	29	4.9	3.3	7.0
	Related	290	104	35.9	30.3	41.7	296	106	35.8	30.3	41.6	586	210	35.8	31.9	39.9
	Grade 2 or 3 Related	290	46	15.9	11.9	20.6	296	39	13.2	9.5	17.6	586	85	14.5	11.8	17.6
	Grade 3 Related	290	12	4.1	2.2	7.1	296	11	3.7	1.9	6.6	586	23	3.9	2.5	5.8
	Medical advice	290	14	4.8	2.7	8.0	296	7	2.4	1.0	4.8	586	21	3.6	2.2	5.4
Loss of appetite	All	290	99	34.1	28.7	39.9	296	100	33.8	28.4	39.5	586	199	34.0	30.1	38.0
	Grade 2 or 3	290	43	14.8	10.9	19.4	296	33	11.1	7.8	15.3	586	76	13.0	10.4	16.0
	Grade 3	290	16	5.5	3.2	8.8	296	14	4.7	2.6	7.8	586	30	5.1	3.5	7.2
	Related	290	84	29.0	23.8	34.6	296	83	28.0	23.0	33.5	586	167	28.5	24.9	32.3
	Grade 2 or 3 Related	290	37	12.8	9.1	17.2	296	27	9.1	6.1	13.0	586	64	10.9	8.5	13.7
	Grade 3 Related	290	16	5.5	3.2	8.8	296	11	3.7	1.9	6.6	586	27	4.6	3.1	6.6
	Medical advice	290	14	4.8	2.7	8.0	296	8	2.7	1.2	5.3	586	22	3.8	2.4	5.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 99 Incidence of solicited symptoms (fever) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total Vaccinated cohort)

		Q-QIV					D-TIV-YB					Total				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Temperature/(Axillary) (°C)	All	289	44	15.2	11.3	19.9	296	44	14.9	11.0	19.4	585	88	15.0	12.2	18.2
	≥38	289	42	14.5	10.7	19.1	296	43	14.5	10.7	19.1	585	85	14.5	11.8	17.6
	≥38.5	289	21	7.3	4.6	10.9	296	22	7.4	4.7	11.0	585	43	7.4	5.4	9.8
	≥39.0	289	11	3.8	1.9	6.7	296	9	3.0	1.4	5.7	585	20	3.4	2.1	5.2
	≥40.0	289	1	0.3	0.0	1.9	296	2	0.7	0.1	2.4	585	3	0.5	0.1	1.5
	Related	289	33	11.4	8.0	15.7	296	31	10.5	7.2	14.5	585	64	10.9	8.5	13.8
	≥38 Related	289	31	10.7	7.4	14.9	296	30	10.1	6.9	14.2	585	61	10.4	8.1	13.2
	≥38.5 Related	289	17	5.9	3.5	9.3	296	13	4.4	2.4	7.4	585	30	5.1	3.5	7.2
	≥39.0 Related	289	8	2.8	1.2	5.4	296	5	1.7	0.6	3.9	585	13	2.2	1.2	3.8
	≥40.0 Related	289	1	0.3	0.0	1.9	296	1	0.3	0.0	1.9	585	2	0.3	0.0	1.2
Dose 2																
Temperature/(Axillary) (°C)	All	272	31	11.4	7.9	15.8	276	25	9.1	5.9	13.1	548	56	10.2	7.8	13.1
	≥38	272	28	10.3	7.0	14.5	276	25	9.1	5.9	13.1	548	53	9.7	7.3	12.5
	≥38.5	272	22	8.1	5.1	12.0	276	13	4.7	2.5	7.9	548	35	6.4	4.5	8.8
	≥39.0	272	12	4.4	2.3	7.6	276	5	1.8	0.6	4.2	548	17	3.1	1.8	4.9
	≥40.0	272	2	0.7	0.1	2.6	276	1	0.4	0.0	2.0	548	3	0.5	0.1	1.6
	Related	272	24	8.8	5.7	12.8	276	21	7.6	4.8	11.4	548	45	8.2	6.1	10.8
	≥38 Related	272	22	8.1	5.1	12.0	276	21	7.6	4.8	11.4	548	43	7.8	5.7	10.4
	≥38.5 Related	272	18	6.6	4.0	10.3	276	10	3.6	1.8	6.6	548	28	5.1	3.4	7.3
	≥39.0 Related	272	9	3.3	1.5	6.2	276	4	1.4	0.4	3.7	548	13	2.4	1.3	4.0
	≥40.0 Related	272	1	0.4	0.0	2.0	276	1	0.4	0.0	2.0	548	2	0.4	0.0	1.3
Overall/dose																
Temperature/(Axillary) (°C)	All	561	75	13.4	10.7	16.5	572	69	12.1	9.5	15.0	1133	144	12.7	10.8	14.8
	≥38	561	70	12.5	9.9	15.5	572	68	11.9	9.4	14.8	1133	138	12.2	10.3	14.2
	≥38.5	561	43	7.7	5.6	10.2	572	35	6.1	4.3	8.4	1133	78	6.9	5.5	8.5
	≥39.0	561	23	4.1	2.6	6.1	572	14	2.4	1.3	4.1	1133	37	3.3	2.3	4.5
	≥40.0	561	3	0.5	0.1	1.6	572	3	0.5	0.1	1.5	1133	6	0.5	0.2	1.1
	Related	561	57	10.2	7.8	13.0	572	52	9.1	6.9	11.8	1133	109	9.6	8.0	11.5
	≥38 Related	561	53	9.4	7.2	12.2	572	51	8.9	6.7	11.6	1133	104	9.2	7.6	11.0
	≥38.5 Related	561	35	6.2	4.4	8.6	572	23	4.0	2.6	6.0	1133	58	5.1	3.9	6.6
	≥39.0 Related	561	17	3.0	1.8	4.8	572	9	1.6	0.7	3.0	1133	26	2.3	1.5	3.3
	≥40.0 Related	561	2	0.4	0.0	1.3	572	2	0.3	0.0	1.3	1133	4	0.4	0.1	0.9
Overall/subject																
Temperature/(Axillary) (°C)	All	290	66	22.8	18.1	28.0	296	61	20.6	16.1	25.7	586	127	21.7	18.4	25.2
	≥38	290	61	21.0	16.5	26.2	296	60	20.3	15.8	25.3	586	121	20.6	17.4	24.2
	≥38.5	290	40	13.8	10.0	18.3	296	33	11.1	7.8	15.3	586	73	12.5	9.9	15.4
	≥39.0	290	23	7.9	5.1	11.7	296	13	4.4	2.4	7.4	586	36	6.1	4.3	8.4
	≥40.0	290	3	1.0	0.2	3.0	296	3	1.0	0.2	2.9	586	6	1.0	0.4	2.2
	Related	290	49	16.9	12.8	21.7	296	48	16.2	12.2	20.9	586	97	16.6	13.6	19.8
	≥38 Related	290	45	15.5	11.5	20.2	296	47	15.9	11.9	20.5	586	92	15.7	12.8	18.9
	≥38.5 Related	290	32	11.0	7.7	15.2	296	23	7.8	5.0	11.4	586	55	9.4	7.1	12.0
	≥39.0 Related	290	17	5.9	3.5	9.2	296	9	3.0	1.4	5.7	586	26	4.4	2.9	6.4
	≥40.0 Related	290	2	0.7	0.1	2.5	296	2	0.7	0.1	2.4	586	4	0.7	0.2	1.7

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine

For each dose and overall/subject: N= number of subjects with at least one documented dose; n/%= number/percentage of subjects reporting the symptom at least once

For Overall/dose: N= number of documented doses; n/%= number/percentage of doses followed by at least one type of symptom; 95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 100 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		142	47.5	41.7	53.3	165	54.6	48.8	60.3
---------- ( )	---------- ( )	0	0.0	0.0	1.2	2*	0.7	0.1	2.4
Ear and labyrinth disorders (10013993)	Ear haemorrhage (10014009)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Ear pain (10014020)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Eye disorders (10015919)	Conjunctivitis (10010741)	3	1.0	0.2	2.9	1	0.3	0.0	1.8
	Lacrimation increased (10023644)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Diarrhoea (10012735)	38	12.7	9.2	17.0	38	12.6	9.1	16.9
	Diarrhoea haemorrhagic (10012741)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Enteritis (10014866)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Faeces hard (10016101)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Flatulence (10016766)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Stomatitis (10042128)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Teething (10043183)	9	3.0	1.4	5.6	7	2.3	0.9	4.7
	Vomiting (10047700)	7	2.3	0.9	4.8	7	2.3	0.9	4.7
General disorders and administration site conditions (10018065)	Injection site erosion (10022059)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Injection site haematoma (10022066)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Injection site rash (10022094)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Irritability (10022998)	0	0.0	0.0	1.2	4	1.3	0.4	3.4
	Pyrexia (10037660)	6	2.0	0.7	4.3	10	3.3	1.6	6.0
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Acute sinusitis (10001076)	4	1.3	0.4	3.4	3	1.0	0.2	2.9
	Acute tonsillitis (10001093)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Ascariasis (10003442)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Blastocystis infection (10005092)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Bronchiolitis (10006448)	4	1.3	0.4	3.4	4	1.3	0.4	3.4
	Bronchitis (10006451)	2	0.7	0.1	2.4	2	0.7	0.1	2.4
	Bronchopneumonia (10006469)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Bullous impetigo (10006563)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Cellulitis (10007882)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	1.2	3	1.0	0.2	2.9
	Croup infectious (10011416)	2	0.7	0.1	2.4	1	0.3	0.0	1.8
	Cutaneous larva migrans (10059547)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Dengue fever (10012310)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Dysentery (10051402)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Ear infection (10014011)	1	0.3	0.0	1.8	6	2.0	0.7	4.3
	Gastroenteritis (10017888)	12	4.0	2.1	6.9	7	2.3	0.9	4.7

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Gingivitis (10018292)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Impetigo (10021531)	3	1.0	0.2	2.9	0	0.0	0.0	1.2
	Infection parasitic (10021857)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Injection site cellulitis (10050057)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Laryngitis (10023874)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Lung infection (10061229)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Nasopharyngitis (10028810)	78	26.1	21.2	31.5	90	29.8	24.7	35.3
	Otitis media (10033078)	3	1.0	0.2	2.9	5	1.7	0.5	3.8
	Otitis media acute (10033079)	3	1.0	0.2	2.9	3	1.0	0.2	2.9
	Parasitic gastroenteritis (10067720)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Pharyngitis (10034835)	11	3.7	1.9	6.5	7	2.3	0.9	4.7
	Pharyngitis streptococcal (10034839)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Pneumonia (10035664)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Rhinitis (10039083)	0	0.0	0.0	1.2	4	1.3	0.4	3.4
	Roseola (10039222)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Scarlet fever (10039587)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Sinusitis (10040753)	5	1.7	0.5	3.9	4	1.3	0.4	3.4
	Subcutaneous abscess (10042343)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Tinea pedis (10043873)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Tonsillitis (10044008)	2	0.7	0.1	2.4	3	1.0	0.2	2.9
	Tooth abscess (10044016)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Upper respiratory tract infection (10046306)	7	2.3	0.9	4.8	10	3.3	1.6	6.0
	Viral infection (10047461)	4	1.3	0.4	3.4	2	0.7	0.1	2.4
	Viral upper respiratory tract infection (10047482)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Face injury (10050392)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Joint injury (10060820)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Lethargy (10024264)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.2	3	1.0	0.2	2.9
	Bronchial hyperreactivity (10066091)	5	1.7	0.5	3.9	5	1.7	0.5	3.8
	Cough (10011224)	13	4.3	2.3	7.3	5	1.7	0.5	3.8
	Nasal congestion (10028735)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Rhinitis allergic (10039085)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Rhinorrhoea (10039101)	2	0.7	0.1	2.4	4	1.3	0.4	3.4

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	2	0.7	0.1	2.4	1	0.3	0.0	1.8
	Dermatitis (10012431)	2	0.7	0.1	2.4	0	0.0	0.0	1.2
	Dermatitis contact (10012442)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Dermatitis diaper (10012444)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Dermatosis (10048768)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Dry skin (10013786)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Ecchymosis (10014080)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Eczema (10014184)	1	0.3	0.0	1.8	3	1.0	0.2	2.9
	Erythema (10015150)	1	0.3	0.0	1.8	3	1.0	0.2	2.9
	Onychoclasis (10048886)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Prurigo (10037083)	3	1.0	0.2	2.9	2	0.7	0.1	2.4
	Rash (10037844)	1	0.3	0.0	1.8	4	1.3	0.4	3.4
	Rash generalised (10037858)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Swelling face (10042682)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Urticaria (10046735)	2	0.7	0.1	2.4	2	0.7	0.1	2.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The 2 AEs for group Q-QIV indicated by "----------" correspond to AE descriptions = "FEVER" and "PARASISTISM" which were not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 101 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		193	33.5	29.7	37.5	209	35.8	32.0	39.9
---------- ( )	---------- ( )	0	0.0	0.0	0.6	2*	0.3	0.0	1.2
Ear and labyrinth disorders (10013993)	Ear haemorrhage (10014009)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Ear pain (10014020)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Eye disorders (10015919)	Conjunctivitis (10010741)	3	0.5	0.1	1.5	1	0.2	0.0	1.0
	Lacrimation increased (10023644)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Diarrhoea (10012735)	43	7.5	5.5	9.9	42	7.2	5.2	9.6
	Diarrhoea haemorrhagic (10012741)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Enteritis (10014866)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Faeces hard (10016101)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Flatulence (10016766)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Stomatitis (10042128)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Teething (10043183)	12	2.1	1.1	3.6	8	1.4	0.6	2.7
	Vomiting (10047700)	8	1.4	0.6	2.7	7	1.2	0.5	2.5
General disorders and administration site conditions (10018065)	Injection site erosion (10022059)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Injection site haematoma (10022066)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Injection site rash (10022094)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Irritability (10022998)	0	0.0	0.0	0.6	4	0.7	0.2	1.7
	Pyrexia (10037660)	6	1.0	0.4	2.3	11	1.9	0.9	3.4
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Acute sinusitis (10001076)	4	0.7	0.2	1.8	3	0.5	0.1	1.5
	Acute tonsillitis (10001093)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Ascariasis (10003442)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Blastocystis infection (10005092)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Bronchiolitis (10006448)	4	0.7	0.2	1.8	4	0.7	0.2	1.7
	Bronchitis (10006451)	2	0.3	0.0	1.2	2	0.3	0.0	1.2
	Bronchopneumonia (10006469)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Bullous impetigo (10006563)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Cellulitis (10007882)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	0.6	3	0.5	0.1	1.5
	Croup infectious (10011416)	2	0.3	0.0	1.2	1	0.2	0.0	1.0
	Cutaneous larva migrans (10059547)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dengue fever (10012310)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dysentery (10051402)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Ear infection (10014011)	1	0.2	0.0	1.0	7	1.2	0.5	2.5
	Gastroenteritis (10017888)	12	2.1	1.1	3.6	7	1.2	0.5	2.5
	Gingivitis (10018292)	1	0.2	0.0	1.0	0	0.0	0.0	0.6

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Impetigo (10021531)	3	0.5	0.1	1.5	0	0.0	0.0	0.6
	Infection parasitic (10021857)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Injection site cellulitis (10050057)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Laryngitis (10023874)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Lung infection (10061229)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Nasopharyngitis (10028810)	93	16.1	13.2	19.4	103	17.7	14.7	21.0
	Otitis media (10033078)	3	0.5	0.1	1.5	5	0.9	0.3	2.0
	Otitis media acute (10033079)	4	0.7	0.2	1.8	3	0.5	0.1	1.5
	Parasitic gastroenteritis (10067720)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
	Pharyngitis (10034835)	13	2.3	1.2	3.8	7	1.2	0.5	2.5
	Pharyngitis streptococcal (10034839)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Pneumonia (10035664)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rhinitis (10039083)	0	0.0	0.0	0.6	4	0.7	0.2	1.7
	Roseola (10039222)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Scarlet fever (10039587)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Sinusitis (10040753)	5	0.9	0.3	2.0	4	0.7	0.2	1.7
	Subcutaneous abscess (10042343)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Tinea pedis (10043873)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Tonsillitis (10044008)	2	0.3	0.0	1.2	3	0.5	0.1	1.5
	Tooth abscess (10044016)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Upper respiratory tract infection (10046306)	8	1.4	0.6	2.7	11	1.9	0.9	3.4
	Viral infection (10047461)	5	0.9	0.3	2.0	2	0.3	0.0	1.2
	Viral upper respiratory tract infection (10047482)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Face injury (10050392)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Joint injury (10060820)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Lethargy (10024264)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.6	3	0.5	0.1	1.5
	Bronchial hyperreactivity (10066091)	5	0.9	0.3	2.0	5	0.9	0.3	2.0
	Cough (10011224)	14	2.4	1.3	4.0	6	1.0	0.4	2.2
	Nasal congestion (10028735)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Rhinitis allergic (10039085)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Rhinorrhoea (10039101)	2	0.3	0.0	1.2	4	0.7	0.2	1.7

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	2	0.3	0.0	1.2	1	0.2	0.0	1.0
	Dermatitis (10012431)	2	0.3	0.0	1.2	0	0.0	0.0	0.6
	Dermatitis contact (10012442)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dermatitis diaper (10012444)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Dermatosis (10048768)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
	Dry skin (10013786)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Ecchymosis (10014080)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Eczema (10014184)	1	0.2	0.0	1.0	3	0.5	0.1	1.5
	Erythema (10015150)	1	0.2	0.0	1.0	3	0.5	0.1	1.5
	Onychoclasis (10048886)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Prurigo (10037083)	3	0.5	0.1	1.5	3	0.5	0.1	1.5
	Rash (10037844)	1	0.2	0.0	1.0	4	0.7	0.2	1.7
	Rash generalised (10037858)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Swelling face (10042682)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Urticaria (10046735)	2	0.3	0.0	1.2	2	0.3	0.0	1.2

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The 2 AEs for group Q-QIV indicated by "----------" correspond to AE descriptions = "FEVER" and "PARASISTISM" which were not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 102 Global Summary of unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

	Group		
	Q-QIV	**D-TIV-YB**	**Total**
Number of subjects with at least one unsolicited symptom reported	142	165	307
Number of doses followed by at least one unsolicited symptom	193	209	402
Number of unsolicited symptoms classified by MedDRA Preferred Term*	295	319	614
Number of unsolicited symptoms reported**	308	327	635

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 103 Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		9	3.0	1.4	5.6	5	1.7	0.5	3.8
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Infections and infestations (10021881)	Croup infectious (10011416)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Ear infection (10014011)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Gastroenteritis (10017888)	4	1.3	0.4	3.4	0	0.0	0.0	1.2
	Nasopharyngitis (10028810)	3	1.0	0.2	2.9	0	0.0	0.0	1.2
	Otitis media acute (10033079)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Tonsillitis (10044008)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Skin and subcutaneous tissue disorders (10040785)	Erythema (10015150)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Rash (10037844)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Urticaria (10046735)	1	0.3	0.0	1.8	0	0.0	0.0	1.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 104 Percentage of doses with grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		10	1.7	0.8	3.2	5	0.9	0.3	2.0
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Infections and infestations (10021881)	Croup infectious (10011416)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Ear infection (10014011)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Gastroenteritis (10017888)	4	0.7	0.2	1.8	0	0.0	0.0	0.6
	Nasopharyngitis (10028810)	3	0.5	0.1	1.5	0	0.0	0.0	0.6
	Otitis media acute (10033079)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Tonsillitis (10044008)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Skin and subcutaneous tissue disorders (10040785)	Erythema (10015150)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Rash (10037844)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Urticaria (10046735)	1	0.2	0.0	1.0	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 105 Global Summary of grade 3 unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

	Group		
	Q-QIV	D-TIV-YB	Total
Number of subjects with at least one unsolicited symptom reported	9	5	14
Number of doses followed by at least one unsolicited symptom	10	5	15
Number of unsolicited symptoms classified by MedDRA Preferred Term*	12	7	19
Number of unsolicited symptoms reported**	13	7	20

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 106 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		17	5.7	3.3	8.9	13	4.3	2.3	7.2
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	5	1.7	0.5	3.9	4	1.3	0.4	3.4
	Faeces hard (10016101)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Vomiting (10047700)	2	0.7	0.1	2.4	4	1.3	0.4	3.4
General disorders and administration site conditions (10018065)	Injection site rash (10022094)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Pyrexia (10037660)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Ear infection (10014011)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Injection site cellulitis (10050057)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Nasopharyngitis (10028810)	5	1.7	0.5	3.9	2	0.7	0.1	2.4
	Upper respiratory tract infection (10046306)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	2	0.7	0.1	2.4	1	0.3	0.0	1.8
	Nasal congestion (10028735)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Rhinorrhoea (10039101)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Erythema (10015150)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Rash (10037844)	0	0.0	0.0	1.2	1	0.3	0.0	1.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 107 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		18	3.1	1.9	4.9	14	2.4	1.3	4.0
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	5	0.9	0.3	2.0	4	0.7	0.2	1.7
	Faeces hard (10016101)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Vomiting (10047700)	2	0.3	0.0	1.2	4	0.7	0.2	1.7
General disorders and administration site conditions (10018065)	Injection site rash (10022094)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Pyrexia (10037660)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Ear infection (10014011)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Injection site cellulitis (10050057)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Nasopharyngitis (10028810)	5	0.9	0.3	2.0	2	0.3	0.0	1.2
	Upper respiratory tract infection (10046306)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	2	0.3	0.0	1.2	2	0.3	0.0	1.2
	Nasal congestion (10028735)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Rhinorrhoea (10039101)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Erythema (10015150)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rash (10037844)	0	0.0	0.0	0.6	1	0.2	0.0	1.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 108 Global Summary of unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

	Group		
	Q-QIV	D-TIV-YB	Total
Number of subjects with at least one unsolicited symptom reported	17	13	30
Number of doses followed by at least one unsolicited symptom	18	14	32
Number of unsolicited symptoms classified by MedDRA Preferred Term*	23	21	44
Number of unsolicited symptoms reported**	25	22	47

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 109 Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.3	0.0	1.8	0	0.0	0.0	1.2
Infections and infestations (10021881)	Nasopharyngitis (10028810)	1	0.3	0.0	1.8	0	0.0	0.0	1.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 110 Percentage of doses with grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.2	0.0	1.0	0	0.0	0.0	0.6
Infections and infestations (10021881)	Nasopharyngitis (10028810)	1	0.2	0.0	1.0	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 111 Global Summary of grade 3 unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

	Group		
	Q-QIV	D-TIV-YB	Total
Number of subjects with at least one unsolicited symptom reported	1	0	1
Number of doses followed by at least one unsolicited symptom	1	0	1
Number of unsolicited symptoms classified by MedDRA Preferred Term*	1	0	1
Number of unsolicited symptoms reported**	1	0	1

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 112 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		97	32.4	27.2	38.1	101	33.4	28.1	39.1
---------- ( )	---------- ( )	0	0.0	0.0	1.2	1*	0.3	0.0	1.8
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Eye disorders (10015919)	Conjunctivitis (10010741)	2	0.7	0.1	2.4	0	0.0	0.0	1.2
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	18	6.0	3.6	9.3	22	7.3	4.6	10.8
	Diarrhoea haemorrhagic (10012741)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Stomatitis (10042128)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Vomiting (10047700)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	4	1.3	0.4	3.4	1	0.3	0.0	1.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Acute sinusitis (10001076)	4	1.3	0.4	3.4	3	1.0	0.2	2.9
	Acute tonsillitis (10001093)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Ascariasis (10003442)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Blastocystis infection (10005092)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Bronchiolitis (10006448)	4	1.3	0.4	3.4	4	1.3	0.4	3.4
	Bronchitis (10006451)	2	0.7	0.1	2.4	2	0.7	0.1	2.4
	Bronchopneumonia (10006469)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Bullous impetigo (10006563)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Cellulitis (10007882)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	1.2	3	1.0	0.2	2.9
	Croup infectious (10011416)	2	0.7	0.1	2.4	0	0.0	0.0	1.2
	Cutaneous larva migrans (10059547)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Dengue fever (10012310)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Dysentery (10051402)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Ear infection (10014011)	1	0.3	0.0	1.8	6	2.0	0.7	4.3
	Gastroenteritis (10017888)	8	2.7	1.2	5.2	5	1.7	0.5	3.8
	Gingivitis (10018292)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Impetigo (10021531)	2	0.7	0.1	2.4	0	0.0	0.0	1.2
	Injection site cellulitis (10050057)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Laryngitis (10023874)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Lung infection (10061229)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Nasopharyngitis (10028810)	52	17.4	13.3	22.2	54	17.9	13.7	22.7
	Otitis media (10033078)	3	1.0	0.2	2.9	4	1.3	0.4	3.4
	Otitis media acute (10033079)	3	1.0	0.2	2.9	3	1.0	0.2	2.9
	Parasitic gastroenteritis (10067720)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Pharyngitis (10034835)	11	3.7	1.9	6.5	6	2.0	0.7	4.3

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Pharyngitis streptococcal (10034839)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Rhinitis (10039083)	0	0.0	0.0	1.2	4	1.3	0.4	3.4
	Scarlet fever (10039587)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Sinusitis (10040753)	5	1.7	0.5	3.9	4	1.3	0.4	3.4
	Tinea pedis (10043873)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Tonsillitis (10044008)	2	0.7	0.1	2.4	3	1.0	0.2	2.9
	Tooth abscess (10044016)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Upper respiratory tract infection (10046306)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Viral infection (10047461)	2	0.7	0.1	2.4	1	0.3	0.0	1.8
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Face injury (10050392)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Joint injury (10060820)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.2	3	1.0	0.2	2.9
	Bronchial hyperreactivity (10066091)	5	1.7	0.5	3.9	5	1.7	0.5	3.8
	Cough (10011224)	1	0.3	0.0	1.8	2	0.7	0.1	2.4
	Rhinitis allergic (10039085)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Dermatosis (10048768)	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Eczema (10014184)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Onychoclasis (10048886)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Prurigo (10037083)	3	1.0	0.2	2.9	2	0.7	0.1	2.4
	Rash (10037844)	0	0.0	0.0	1.2	2	0.7	0.1	2.4
	Urticaria (10046735)	2	0.7	0.1	2.4	2	0.7	0.1	2.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" which was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 113 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		119	20.7	17.4	24.2	111	19.0	15.9	22.5
---------- ( )	---------- ( )	0	0.0	0.0	0.6	1*	0.2	0.0	1.0
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Eye disorders (10015919)	Conjunctivitis (10010741)	2	0.3	0.0	1.2	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	18	3.1	1.9	4.9	22	3.8	2.4	5.7
	Diarrhoea haemorrhagic (10012741)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Stomatitis (10042128)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Vomiting (10047700)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	4	0.7	0.2	1.8	1	0.2	0.0	1.0
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Acute sinusitis (10001076)	4	0.7	0.2	1.8	3	0.5	0.1	1.5
	Acute tonsillitis (10001093)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Ascariasis (10003442)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Blastocystis infection (10005092)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Bronchiolitis (10006448)	4	0.7	0.2	1.8	4	0.7	0.2	1.7
	Bronchitis (10006451)	2	0.3	0.0	1.2	2	0.3	0.0	1.2
	Bronchopneumonia (10006469)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Bullous impetigo (10006563)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Cellulitis (10007882)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	0.6	3	0.5	0.1	1.5
	Croup infectious (10011416)	2	0.3	0.0	1.2	0	0.0	0.0	0.6
	Cutaneous larva migrans (10059547)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dengue fever (10012310)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dysentery (10051402)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Ear infection (10014011)	1	0.2	0.0	1.0	7	1.2	0.5	2.5
	Gastroenteritis (10017888)	8	1.4	0.6	2.7	5	0.9	0.3	2.0
	Gingivitis (10018292)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Impetigo (10021531)	2	0.3	0.0	1.2	0	0.0	0.0	0.6
	Injection site cellulitis (10050057)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Laryngitis (10023874)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Lung infection (10061229)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Nasopharyngitis (10028810)	57	9.9	7.6	12.6	56	9.6	7.3	12.3
	Otitis media (10033078)	3	0.5	0.1	1.5	4	0.7	0.2	1.7
	Otitis media acute (10033079)	3	0.5	0.1	1.5	3	0.5	0.1	1.5
	Parasitic gastroenteritis (10067720)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Pharyngitis (10034835)	13	2.3	1.2	3.8	6	1.0	0.4	2.2

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Pharyngitis streptococcal (10034839)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rhinitis (10039083)	0	0.0	0.0	0.6	4	0.7	0.2	1.7
	Scarlet fever (10039587)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Sinusitis (10040753)	5	0.9	0.3	2.0	4	0.7	0.2	1.7
	Tinea pedis (10043873)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Tonsillitis (10044008)	2	0.3	0.0	1.2	3	0.5	0.1	1.5
	Tooth abscess (10044016)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Upper respiratory tract infection (10046306)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Viral infection (10047461)	2	0.3	0.0	1.2	1	0.2	0.0	1.0
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Face injury (10050392)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Joint injury (10060820)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.6	3	0.5	0.1	1.5
	Bronchial hyperreactivity (10066091)	5	0.9	0.3	2.0	5	0.9	0.3	2.0
	Cough (10011224)	1	0.2	0.0	1.0	2	0.3	0.0	1.2
	Rhinitis allergic (10039085)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Dermatosis (10048768)	1	0.2	0.0	1.0	1	0.2	0.0	1.0
	Eczema (10014184)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Onychoclasis (10048886)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Prurigo (10037083)	3	0.5	0.1	1.5	3	0.5	0.1	1.5
	Rash (10037844)	0	0.0	0.0	0.6	2	0.3	0.0	1.2
	Urticaria (10046735)	2	0.3	0.0	1.2	2	0.3	0.0	1.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" which was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 114 Global Summary of unsolicited adverse events reported with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

	Group		
	Q-QIV	D-TIV-YB	Total
Number of subjects with at least one unsolicited symptom reported	97	101	198
Number of doses followed by at least one unsolicited symptom	119	111	230
Number of unsolicited symptoms classified by MedDRA Preferred Term*	163	168	331
Number of unsolicited symptoms reported**	166	168	334

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 115 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 299				D-TIV-YB N = 302			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.3	0.0	1.8	2	0.7	0.1	2.4
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Infections and infestations (10021881)	Blastocystis infection (10005092)	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Bronchiolitis (10006448)	0	0.0	0.0	1.2	2	0.7	0.1	2.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 116 Percentage of doses with serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

		Q-QIV N = 576				D-TIV-YB N = 583			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.2	0.0	1.0	2	0.3	0.0	1.2
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Infections and infestations (10021881)	Blastocystis infection (10005092)	0	0.0	0.0	0.6	1	0.2	0.0	1.0
	Bronchiolitis (10006448)	0	0.0	0.0	0.6	2	0.3	0.0	1.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 117 Global Summary of serious adverse events reported within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

	Group		
	Q-QIV	D-TIV-YB	Total
Number of subjects with at least one unsolicited symptom reported	1	2	3
Number of doses followed by at least one unsolicited symptom	1	2	3
Number of unsolicited symptoms classified by MedDRA Preferred Term*	1	3	4
Number of unsolicited symptoms reported**	1	3	4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 118 Percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

No records exist in this table

Table 119 Listing of potential Immune-Mediated Disease reported within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

No records exist in this table

Table 120 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom during the 7-day post-vaccination period (Total Vaccinated cohort)

								Relative Risk (Q-QIV over D-TIV-YB)			
		Q-QIV			D-TIV-YB				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Drowsiness	All	289	72	24.9	296	64	21.6	1.15	0.86	1.55	0.3787
	Grade 3	289	6	2.1	296	4	1.4	1.54	0.47	5.03	0.5409
Irritability / fussiness	All	289	91	31.5	296	94	31.8	0.99	0.78	1.26	1.0000
	Grade 3	289	11	3.8	296	10	3.4	1.13	0.50	2.56	0.8270
Loss of appetite	All	289	78	27.0	296	71	24.0	1.13	0.85	1.49	0.4479
	Grade 3	289	9	3.1	296	7	2.4	1.32	0.51	3.37	0.6206
Dose 2											
Drowsiness	All	272	49	18.0	276	44	15.9	1.13	0.78	1.64	0.5698
	Grade 3	272	3	1.1	276	5	1.8	0.61	0.16	2.29	0.7246
Irritability / fussiness	All	272	72	26.5	276	75	27.2	0.97	0.74	1.28	0.9232
	Grade 3	272	6	2.2	276	5	1.8	1.22	0.40	3.72	0.7707
Loss of appetite	All	272	48	17.6	276	55	19.9	0.89	0.63	1.25	0.5133
	Grade 3	272	8	2.9	276	8	2.9	1.01	0.40	2.58	1.0000
Overall/dose											
Drowsiness	All	561	121	21.6	572	108	18.9	1.14	0.91	1.44	0.2679
	Grade 3	561	9	1.6	572	9	1.6	1.02	0.42	2.48	1.0000
Irritability / fussiness	All	561	163	29.1	572	169	29.5	0.98	0.82	1.18	0.8962
	Grade 3	561	17	3.0	572	15	2.6	1.16	0.59	2.26	0.7224
Loss of appetite	All	561	126	22.5	572	126	22.0	1.02	0.82	1.27	0.8865
	Grade 3	561	17	3.0	572	15	2.6	1.16	0.59	2.26	0.7224
Overall/subject											
Drowsiness	All	290	93	32.1	296	88	29.7	1.08	0.85	1.37	0.5917
	Grade 3	290	9	3.1	296	9	3.0	1.02	0.42	2.46	1.0000
Irritability / fussiness	All	290	118	40.7	296	123	41.6	0.98	0.81	1.19	0.8668
	Grade 3	290	15	5.2	296	14	4.7	1.09	0.54	2.20	0.8506
Loss of appetite	All	290	99	34.1	296	100	33.8	1.01	0.81	1.27	0.9307
	Grade 3	290	16	5.5	296	14	4.7	1.17	0.59	2.32	0.7106

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 121 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited local symptom during the 7-day post-vaccination period (Total Vaccinated cohort)

								Relative Risk (Q-QIV over D-TIV-YB)			
		Q-QIV			D-TIV-YB				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Dose 1											
Pain	All	290	73	25.2	297	64	21.5	1.17	0.87	1.57	0.3295
	Grade 3	290	5	1.7	297	1	0.3	5.12	0.80	33.00	0.1191
Redness (mm)	All	290	3	1.0	297	2	0.7	1.54	0.31	7.65	0.6828
	>100	290	0	0.0	297	0	0.0	INF	0.00	INF	
Swelling (mm)	All	290	2	0.7	297	2	0.7	1.02	0.18	5.78	1.0000
	>100	290	0	0.0	297	0	0.0	INF	0.00	INF	
Dose 2											
Pain	All	274	57	20.8	276	59	21.4	0.97	0.70	1.34	0.9169
	Grade 3	274	3	1.1	276	3	1.1	1.01	0.23	4.34	1.0000
Redness (mm)	All	274	4	1.5	276	4	1.4	1.01	0.28	3.65	1.0000
	>100	274	0	0.0	276	0	0.0	INF	0.00	INF	
Swelling (mm)	All	274	4	1.5	276	5	1.8	0.81	0.24	2.75	1.0000
	>100	274	0	0.0	276	0	0.0	INF	0.00	INF	
Overall/dose											
Pain	All	564	130	23.0	573	123	21.5	1.07	0.86	1.33	0.5221
	Grade 3	564	8	1.4	573	4	0.7	2.03	0.65	6.32	0.2608
Redness (mm)	All	564	7	1.2	573	6	1.0	1.19	0.42	3.35	0.7878
	>100	564	0	0.0	573	0	0.0	INF	0.00	INF	
Swelling (mm)	All	564	6	1.1	573	7	1.2	0.87	0.31	2.46	1.0000
	>100	564	0	0.0	573	0	0.0	INF	0.00	INF	
Overall/subject											
Pain	All	291	95	32.6	297	91	30.6	1.07	0.84	1.35	0.6575
	Grade 3	291	7	2.4	297	3	1.0	2.38	0.68	8.40	0.2183
Redness (mm)	All	291	6	2.1	297	6	2.0	1.02	0.35	2.97	1.0000
	>100	291	0	0.0	297	0	0.0	INF	0.00	INF	
Swelling (mm)	All	291	5	1.7	297	6	2.0	0.85	0.28	2.60	1.0000
	>100	291	0	0.0	297	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 122 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 48 hours of the vaccinations (Total Vaccinated cohort)

								Relative Risk (Q-QIV over D-TIV-YB)			
		Q-QIV			D-TIV-YB				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	289	22	7.6	296	18	6.1	1.25	0.69	2.27	0.5142
	≥38	289	19	6.6	296	17	5.7	1.14	0.61	2.14	0.7324
	≥38.5	289	9	3.1	296	6	2.0	1.54	0.58	4.10	0.4438
	≥39.0	289	4	1.4	296	2	0.7	2.05	0.44	9.52	0.4456
	≥40.0	289	0	0.0	296	0	0.0	INF	0.00	INF	
	Related	289	21	7.3	296	17	5.7	1.27	0.69	2.33	0.5044
	≥38 Related	289	18	6.2	296	16	5.4	1.15	0.61	2.19	0.7257
	≥38.5 Related	289	8	2.8	296	5	1.7	1.64	0.57	4.72	0.4137
	≥39.0 Related	289	3	1.0	296	2	0.7	1.54	0.31	7.66	0.6827
	≥40.0 Related	289	0	0.0	296	0	0.0	INF	0.00	INF	
Dose 2											
Temperature/(Axillary) (°C)	All	272	16	5.9	276	12	4.3	1.35	0.66	2.77	0.4436
	≥38	272	16	5.9	276	12	4.3	1.35	0.66	2.77	0.4436
	≥38.5	272	10	3.7	276	2	0.7	5.07	1.26	20.51	0.0203
	≥39.0	272	5	1.8	276	1	0.4	5.07	0.79	32.69	0.1206
	≥40.0	272	0	0.0	276	0	0.0	INF	0.00	INF	
	Related	272	15	5.5	276	11	4.0	1.38	0.66	2.91	0.4280
	≥38 Related	272	15	5.5	276	11	4.0	1.38	0.66	2.91	0.4280
	≥38.5 Related	272	9	3.3	276	1	0.4	9.13	1.51	55.65	0.0106
	≥39.0 Related	272	4	1.5	276	0	0.0	INF	1.06	INF	0.0600
	≥40.0 Related	272	0	0.0	276	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	561	38	6.8	572	30	5.2	1.29	0.82	2.05	0.3174
	≥38	561	35	6.2	572	29	5.1	1.23	0.77	1.98	0.4408
	≥38.5	561	19	3.4	572	8	1.4	2.42	1.09	5.38	0.0321
	≥39.0	561	9	1.6	572	3	0.5	3.06	0.90	10.41	0.0878
	≥40.0	561	0	0.0	572	0	0.0	INF	0.00	INF	
	Related	561	36	6.4	572	28	4.9	1.31	0.82	2.11	0.3038
	≥38 Related	561	33	5.9	572	27	4.7	1.25	0.76	2.04	0.4269
	≥38.5 Related	561	17	3.0	572	6	1.0	2.89	1.18	7.07	0.0203
	≥39.0 Related	561	7	1.2	572	2	0.3	3.57	0.85	15.08	0.1049
	≥40.0 Related	561	0	0.0	572	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	290	33	11.4	296	29	9.8	1.16	0.73	1.86	0.5918
	≥38	290	30	10.3	296	28	9.5	1.09	0.67	1.78	0.7826
	≥38.5	290	18	6.2	296	8	2.7	2.30	1.04	5.10	0.0453
	≥39.0	290	9	3.1	296	3	1.0	3.06	0.91	10.40	0.0862
	≥40.0	290	0	0.0	296	0	0.0	INF	0.00	INF	
	Related	290	31	10.7	296	27	9.1	1.17	0.72	1.91	0.5809
	≥38 Related	290	28	9.7	296	26	8.8	1.10	0.66	1.82	0.7758
	≥38.5 Related	290	16	5.5	296	6	2.0	2.72	1.12	6.67	0.0300
	≥39.0 Related	290	7	2.4	296	2	0.7	3.57	0.85	15.06	0.1035
	≥40.0 Related	290	0	0.0	296	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
For each dose and overall/subject:

N = number of subjects with at least one documented dosen/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 123 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 4 days post-vaccinations (Total Vaccinated cohort)

								Relative Risk (Q-QIV over D-TIV-YB)			
		Q-QIV			D-TIV-YB				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	289	33	11.4	296	29	9.8	1.17	0.73	1.86	0.5916
	≥38	289	32	11.1	296	26	8.8	1.26	0.77	2.05	0.4071
	≥38.5	289	15	5.2	296	11	3.7	1.40	0.66	2.94	0.4270
	≥39.0	289	6	2.1	296	4	1.4	1.54	0.47	5.03	0.5409
	≥40.0	289	0	0.0	296	1	0.3	0.00	0.00	3.93	1.0000
	Related	289	28	9.7	296	24	8.1	1.19	0.71	2.00	0.5620
	≥38 Related	289	27	9.3	296	22	7.4	1.26	0.74	2.14	0.4566
	≥38.5 Related	289	13	4.5	296	8	2.7	1.66	0.72	3.87	0.2726
	≥39.0 Related	289	4	1.4	296	3	1.0	1.37	0.34	5.42	0.7219
	≥40.0 Related	289	0	0.0	296	1	0.3	0.00	0.00	3.93	1.0000
Dose 2											
Temperature/(Axillary) (°C)	All	272	22	8.1	276	18	6.5	1.24	0.69	2.24	0.5145
	≥38	272	21	7.7	276	18	6.5	1.18	0.65	2.16	0.6211
	≥38.5	272	16	5.9	276	10	3.6	1.62	0.76	3.46	0.2335
	≥39.0	272	10	3.7	276	4	1.4	2.54	0.85	7.58	0.1115
	≥40.0	272	1	0.4	276	1	0.4	1.01	0.11	9.70	1.0000
	Related	272	17	6.3	276	15	5.4	1.15	0.59	2.23	0.7187
	≥38 Related	272	17	6.3	276	15	5.4	1.15	0.59	2.23	0.7187
	≥38.5 Related	272	13	4.8	276	7	2.5	1.88	0.79	4.53	0.1784
	≥39.0 Related	272	8	2.9	276	3	1.1	2.71	0.79	9.34	0.1395
	≥40.0 Related	272	0	0.0	276	1	0.4	0.00	0.00	3.89	1.0000
Overall/dose											
Temperature/(Axillary) (°C)	All	561	55	9.8	572	47	8.2	1.19	0.82	1.73	0.4064
	≥38	561	53	9.4	572	44	7.7	1.23	0.84	1.80	0.3393
	≥38.5	561	31	5.5	572	21	3.7	1.51	0.88	2.57	0.1561
	≥39.0	561	16	2.9	572	8	1.4	2.04	0.90	4.62	0.1012
	≥40.0	561	1	0.2	572	2	0.3	0.51	0.07	3.88	1.0000
	Related	561	45	8.0	572	39	6.8	1.18	0.78	1.77	0.4965
	≥38 Related	561	44	7.8	572	37	6.5	1.21	0.80	1.84	0.4198
	≥38.5 Related	561	26	4.6	572	15	2.6	1.77	0.96	3.27	0.0803
	≥39.0 Related	561	12	2.1	572	6	1.0	2.04	0.80	5.22	0.1601
	≥40.0 Related	561	0	0.0	572	2	0.3	0.00	0.00	1.96	0.4996
Overall/subject											
Temperature/(Axillary) (°C)	All	290	48	16.6	296	45	15.2	1.09	0.75	1.58	0.7346
	≥38	290	46	15.9	296	42	14.2	1.12	0.76	1.64	0.6439
	≥38.5	290	28	9.7	296	20	6.8	1.43	0.83	2.47	0.2292
	≥39.0	290	16	5.5	296	8	2.7	2.04	0.91	4.60	0.0977
	≥40.0	290	1	0.3	296	2	0.7	0.51	0.07	3.88	1.0000
	Related	290	39	13.4	296	38	12.8	1.05	0.69	1.58	0.9028
	≥38 Related	290	38	13.1	296	36	12.2	1.08	0.71	1.65	0.8038
	≥38.5 Related	290	23	7.9	296	15	5.1	1.57	0.84	2.91	0.1812
	≥39.0 Related	290	12	4.1	296	6	2.0	2.04	0.80	5.20	0.1568
	≥40.0 Related	290	0	0.0	296	2	0.7	0.00	0.00	1.95	0.4992

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose

n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 124 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 7 days post-vaccinations (Total Vaccinated cohort)

								Relative Risk (Q-QIV over D-TIV-YB)			
		Q-QIV			D-TIV-YB				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	289	44	15.2	296	44	14.9	1.02	0.70	1.50	0.9085
	≥38	289	42	14.5	296	43	14.5	1.00	0.68	1.48	1.0000
	≥38.5	289	21	7.3	296	22	7.4	0.98	0.55	1.73	1.0000
	≥39.0	289	11	3.8	296	9	3.0	1.25	0.54	2.91	0.6547
	≥40.0	289	1	0.3	296	2	0.7	0.51	0.07	3.89	1.0000
	Related	289	33	11.4	296	31	10.5	1.09	0.69	1.73	0.7914
	≥38 Related	289	31	10.7	296	30	10.1	1.06	0.66	1.70	0.8926
	≥38.5 Related	289	17	5.9	296	13	4.4	1.34	0.67	2.67	0.4570
	≥39.0 Related	289	8	2.8	296	5	1.7	1.64	0.57	4.72	0.4137
	≥40.0 Related	289	1	0.3	296	1	0.3	1.02	0.11	9.80	1.0000
Dose 2											
Temperature/(Axillary) (°C)	All	272	31	11.4	276	25	9.1	1.26	0.77	2.07	0.3992
	≥38	272	28	10.3	276	25	9.1	1.14	0.68	1.89	0.6661
	≥38.5	272	22	8.1	276	13	4.7	1.72	0.89	3.31	0.1179
	≥39.0	272	12	4.4	276	5	1.8	2.44	0.91	6.57	0.0892
	≥40.0	272	2	0.7	276	1	0.4	2.03	0.27	15.46	0.6216
	Related	272	24	8.8	276	21	7.6	1.16	0.67	2.02	0.6428
	≥38 Related	272	22	8.1	276	21	7.6	1.06	0.60	1.87	0.8747
	≥38.5 Related	272	18	6.6	276	10	3.6	1.83	0.87	3.83	0.1237
	≥39.0 Related	272	9	3.3	276	4	1.4	2.28	0.75	6.93	0.1717
	≥40.0 Related	272	1	0.4	276	1	0.4	1.01	0.11	9.70	1.0000
Overall/dose											
Temperature/(Axillary) (°C)	All	561	75	13.4	572	69	12.1	1.11	0.82	1.50	0.5331
	≥38	561	70	12.5	572	68	11.9	1.05	0.77	1.43	0.7857
	≥38.5	561	43	7.7	572	35	6.1	1.25	0.82	1.92	0.3481
	≥39.0	561	23	4.1	572	14	2.4	1.68	0.88	3.19	0.1337
	≥40.0	561	3	0.5	572	3	0.5	1.02	0.24	4.40	1.0000
	Related	561	57	10.2	572	52	9.1	1.12	0.78	1.60	0.5474
	≥38 Related	561	53	9.4	572	51	8.9	1.06	0.74	1.53	0.7589
	≥38.5 Related	561	35	6.2	572	23	4.0	1.55	0.93	2.58	0.1056
	≥39.0 Related	561	17	3.0	572	9	1.6	1.93	0.88	4.20	0.1148
	≥40.0 Related	561	2	0.4	572	2	0.3	1.02	0.18	5.77	1.0000
Overall/subject											
Temperature/(Axillary) (°C)	All	290	66	22.8	296	61	20.6	1.10	0.81	1.50	0.5485
	≥38	290	61	21.0	296	60	20.3	1.04	0.76	1.42	0.8388
	≥38.5	290	40	13.8	296	33	11.1	1.24	0.81	1.90	0.3815
	≥39.0	290	23	7.9	296	13	4.4	1.81	0.94	3.46	0.0860
	≥40.0	290	3	1.0	296	3	1.0	1.02	0.24	4.40	1.0000
	Related	290	49	16.9	296	48	16.2	1.04	0.73	1.50	0.9115
	≥38 Related	290	45	15.5	296	47	15.9	0.98	0.67	1.42	0.9102
	≥38.5 Related	290	32	11.0	296	23	7.8	1.42	0.86	2.36	0.2028
	≥39.0 Related	290	17	5.9	296	9	3.0	1.93	0.89	4.18	0.1107
	≥40.0 Related	290	2	0.7	296	2	0.7	1.02	0.18	5.76	1.0000

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
For each dose and overall/subject:

N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 125 Incidence of concomitant medication use during the 28-day (Days 0-27) post-vaccination period by dose and overall (Total Vaccinated cohort)

	Q-QIV					D-TIV-YB					Total				
				95% CI					95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1															
Any	299	119	39.8	34.2	45.6	302	130	43.0	37.4	48.8	601	249	41.4	37.5	45.5
Any antipyretic	299	67	22.4	17.8	27.6	302	73	24.2	19.5	29.4	601	140	23.3	20.0	26.9
Prophylactic antipyretic	299	9	3.0	1.4	5.6	302	5	1.7	0.5	3.8	601	14	2.3	1.3	3.9
Dose 2															
Any	277	91	32.9	27.4	38.7	281	98	34.9	29.3	40.8	558	189	33.9	29.9	38.0
Any antipyretic	277	47	17.0	12.7	21.9	281	46	16.4	12.2	21.2	558	93	16.7	13.7	20.0
Prophylactic antipyretic	277	0	0.0	0.0	1.3	281	3	1.1	0.2	3.1	558	3	0.5	0.1	1.6
Overall/dose															
Any	576	210	36.5	32.5	40.5	583	228	39.1	35.1	43.2	1159	438	37.8	35.0	40.7
Any antipyretic	576	114	19.8	16.6	23.3	583	119	20.4	17.2	23.9	1159	233	20.1	17.8	22.5
Prophylactic antipyretic	576	9	1.6	0.7	2.9	583	8	1.4	0.6	2.7	1159	17	1.5	0.9	2.3
Overall/subject															
Any	299	157	52.5	46.7	58.3	302	169	56.0	50.2	61.6	601	326	54.2	50.2	58.3
Any antipyretic	299	95	31.8	26.5	37.4	302	99	32.8	27.5	38.4	601	194	32.3	28.6	36.2
Prophylactic antipyretic	299	9	3.0	1.4	5.6	302	8	2.6	1.2	5.2	601	17	2.8	1.7	4.5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
Total = Total
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

10.3.2. By age strata

Table 126 Number and percentage of subjects who received study vaccine dose(s) (By age strata - Total Vaccinated cohort)

	Q-QIV				D-TIV-YB			
	6-17M N = 157		18-35M N = 142		6-17M N = 160		18-35M N = 142	
Total number of doses received	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
1	2	1.3	20	14.1	6	3.8	15	10.6
2	155	98.7	122	85.9	154	96.3	127	89.4
Any	157	100	142	100	160	100	142	100

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = number of subjects in each group included in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose

Table 127 Compliance in returning symptom sheets (By age strata - Total Vaccinated cohort)

Dose	Group	Sub-group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
1	Q-QIV	6-17M	157	6	154	98.1	154	98.1
		18-35M	142	0	135	95.1	136	95.8
	D-TIV-YB	6-17M	160	4	155	96.9	156	97.5
		18-35M	142	4	141	99.3	141	99.3
2	Q-QIV	6-17M	155	0	151	97.4	153	98.7
		18-35M	122	0	121	99.2	121	99.2
	D-TIV-YB	6-17M	154	0	149	96.8	149	96.8
		18-35M	127	2	127	100	127	100
Total	Q-QIV	6-17M	312	6	305	97.8	307	98.4
		18-35M	264	0	256	97.0	257	97.3
	D-TIV-YB	6-17M	314	4	304	96.8	305	97.1
		18-35M	269	6	268	99.6	268	99.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
SS = Symptom sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom sheet return / number of administered doses) X 100

Table 128 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By age strata - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	78	49.7	41.6	57.8	157	76	48.4	40.4	56.5
		18-35M	142	81	57.0	48.5	65.3	142	73	51.4	42.9	59.9
	D-TIV-YB	6-17M	160	88	55.0	46.9	62.9	160	85	53.1	45.1	61.0
		18-35M	142	81	57.0	48.5	65.3	142	67	47.2	38.8	55.7
Dose 2	Q-QIV	6-17M	155	69	44.5	36.5	52.7	155	62	40.0	32.2	48.2
		18-35M	122	57	46.7	37.6	56.0	122	50	41.0	32.2	50.3
	D-TIV-YB	6-17M	154	63	40.9	33.1	49.1	154	58	37.7	30.0	45.8
		18-35M	127	70	55.1	46.0	63.9	127	60	47.2	38.3	56.3
Overall/dose	Q-QIV	6-17M	312	147	47.1	41.5	52.8	312	138	44.2	38.6	49.9
		18-35M	264	138	52.3	46.1	58.4	264	123	46.6	40.5	52.8
	D-TIV-YB	6-17M	314	151	48.1	42.4	53.8	314	143	45.5	39.9	51.2
		18-35M	269	151	56.1	50.0	62.2	269	127	47.2	41.1	53.4
Overall/subject	Q-QIV	6-17M	157	98	62.4	54.3	70.0	157	94	59.9	51.8	67.6
		18-35M	142	92	64.8	56.3	72.6	142	85	59.9	51.3	68.0
	D-TIV-YB	6-17M	160	104	65.0	57.1	72.4	160	99	61.9	53.9	69.4
		18-35M	142	101	71.1	62.9	78.4	142	90	63.4	54.9	71.3

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	28	17.8	12.2	24.7
		18-35M	142	49	34.5	26.7	42.9
	D-TIV-YB	6-17M	160	21	13.1	8.3	19.4
		18-35M	142	47	33.1	25.4	41.5
Dose 2	Q-QIV	6-17M	155	26	16.8	11.3	23.6
		18-35M	122	32	26.2	18.7	35.0
	D-TIV-YB	6-17M	154	22	14.3	9.2	20.8
		18-35M	127	41	32.3	24.3	41.2
Overall/dose	Q-QIV	6-17M	312	54	17.3	13.3	22.0
		18-35M	264	81	30.7	25.2	36.6
	D-TIV-YB	6-17M	314	43	13.7	10.1	18.0
		18-35M	269	88	32.7	27.1	38.7
Overall/subject	Q-QIV	6-17M	157	41	26.1	19.4	33.7
		18-35M	142	57	40.1	32.0	48.7
	D-TIV-YB	6-17M	160	34	21.3	15.2	28.4
		18-35M	142	62	43.7	35.4	52.2

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 129 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By age strata - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	15	9.6	5.4	15.3	157	15	9.6	5.4	15.3
		18-35M	142	16	11.3	6.6	17.7	142	15	10.6	6.0	16.8
	D-TIV-YB	6-17M	160	16	10.0	5.8	15.7	160	16	10.0	5.8	15.7
		18-35M	142	6	4.2	1.6	9.0	142	6	4.2	1.6	9.0
Dose 2	Q-QIV	6-17M	155	13	8.4	4.5	13.9	155	13	8.4	4.5	13.9
		18-35M	122	11	9.0	4.6	15.6	122	10	8.2	4.0	14.6
	D-TIV-YB	6-17M	154	10	6.5	3.2	11.6	154	9	5.8	2.7	10.8
		18-35M	127	8	6.3	2.8	12.0	127	7	5.5	2.2	11.0
Overall/dose	Q-QIV	6-17M	312	28	9.0	6.0	12.7	312	28	9.0	6.0	12.7
		18-35M	264	27	10.2	6.8	14.5	264	25	9.5	6.2	13.7
	D-TIV-YB	6-17M	314	26	8.3	5.5	11.9	314	25	8.0	5.2	11.5
		18-35M	269	14	5.2	2.9	8.6	269	13	4.8	2.6	8.1
Overall/subject	Q-QIV	6-17M	157	24	15.3	10.0	21.9	157	24	15.3	10.0	21.9
		18-35M	142	23	16.2	10.6	23.3	142	22	15.5	10.0	22.5
	D-TIV-YB	6-17M	160	24	15.0	9.9	21.5	160	24	15.0	9.9	21.5
		18-35M	142	12	8.5	4.4	14.3	142	11	7.7	3.9	13.4

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	2	1.3	0.2	4.5
		18-35M	142	3	2.1	0.4	6.0
	D-TIV-YB	6-17M	160	1	0.6	0.0	3.4
		18-35M	142	0	0.0	0.0	2.6
Dose 2	Q-QIV	6-17M	155	2	1.3	0.2	4.6
		18-35M	122	1	0.8	0.0	4.5
	D-TIV-YB	6-17M	154	1	0.6	0.0	3.6
		18-35M	127	2	1.6	0.2	5.6
Overall/dose	Q-QIV	6-17M	312	4	1.3	0.4	3.2
		18-35M	264	4	1.5	0.4	3.8
	D-TIV-YB	6-17M	314	2	0.6	0.1	2.3
		18-35M	269	2	0.7	0.1	2.7
Overall/subject	Q-QIV	6-17M	157	4	2.5	0.7	6.4
		18-35M	142	3	2.1	0.4	6.0
	D-TIV-YB	6-17M	160	1	0.6	0.0	3.4
		18-35M	142	2	1.4	0.2	5.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 130 Incidence and nature of symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By age strata - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	66	42.0	34.2	50.2	157	61	38.9	31.2	46.9
		18-35M	142	77	54.2	45.7	62.6	142	63	44.4	36.0	52.9
	D-TIV-YB	6-17M	160	69	43.1	35.3	51.2	160	63	39.4	31.8	47.4
		18-35M	142	72	50.7	42.2	59.2	142	52	36.6	28.7	45.1
Dose 2	Q-QIV	6-17M	155	59	38.1	30.4	46.2	155	50	32.3	25.0	40.2
		18-35M	122	51	41.8	32.9	51.1	122	39	32.0	23.8	41.0
	D-TIV-YB	6-17M	154	53	34.4	27.0	42.5	154	48	31.2	24.0	39.1
		18-35M	127	62	48.8	39.9	57.8	127	47	37.0	28.6	46.0
Overall/dose	Q-QIV	6-17M	312	125	40.1	34.6	45.7	312	111	35.6	30.3	41.2
		18-35M	264	128	48.5	42.3	54.7	264	102	38.6	32.7	44.8
	D-TIV-YB	6-17M	314	122	38.9	33.4	44.5	314	111	35.4	30.1	40.9
		18-35M	269	134	49.8	43.7	55.9	269	99	36.8	31.0	42.9
Overall/subject	Q-QIV	6-17M	157	84	53.5	45.4	61.5	157	77	49.0	41.0	57.1
		18-35M	142	86	60.6	52.0	68.7	142	71	50.0	41.5	58.5
	D-TIV-YB	6-17M	160	84	52.5	44.5	60.4	160	79	49.4	41.4	57.4
		18-35M	142	91	64.1	55.6	72.0	142	73	51.4	42.9	59.9

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	28	17.8	12.2	24.7
		18-35M	142	49	34.5	26.7	42.9
	D-TIV-YB	6-17M	160	21	13.1	8.3	19.4
		18-35M	142	46	32.4	24.8	40.8
Dose 2	Q-QIV	6-17M	155	26	16.8	11.3	23.6
		18-35M	122	32	26.2	18.7	35.0
	D-TIV-YB	6-17M	154	21	13.6	8.6	20.1
		18-35M	127	41	32.3	24.3	41.2
Overall/dose	Q-QIV	6-17M	312	54	17.3	13.3	22.0
		18-35M	264	81	30.7	25.2	36.6
	D-TIV-YB	6-17M	314	42	13.4	9.8	17.6
		18-35M	269	87	32.3	26.8	38.3
Overall/subject	Q-QIV	6-17M	157	41	26.1	19.4	33.7
		18-35M	142	57	40.1	32.0	48.7
	D-TIV-YB	6-17M	160	33	20.6	14.6	27.7
		18-35M	142	61	43.0	34.7	51.5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 131 Incidence and nature of grade 3 symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By age strata - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	9	5.7	2.7	10.6	157	9	5.7	2.7	10.6
		18-35M	142	15	10.6	6.0	16.8	142	14	9.9	5.5	16.0
	D-TIV-YB	6-17M	160	10	6.3	3.0	11.2	160	10	6.3	3.0	11.2
		18-35M	142	5	3.5	1.2	8.0	142	5	3.5	1.2	8.0
Dose 2	Q-QIV	6-17M	155	11	7.1	3.6	12.3	155	11	7.1	3.6	12.3
		18-35M	122	7	5.7	2.3	11.5	122	6	4.9	1.8	10.4
	D-TIV-YB	6-17M	154	8	5.2	2.3	10.0	154	7	4.5	1.8	9.1
		18-35M	127	8	6.3	2.8	12.0	127	7	5.5	2.2	11.0
Overall/dose	Q-QIV	6-17M	312	20	6.4	4.0	9.7	312	20	6.4	4.0	9.7
		18-35M	264	22	8.3	5.3	12.3	264	20	7.6	4.7	11.5
	D-TIV-YB	6-17M	314	18	5.7	3.4	8.9	314	17	5.4	3.2	8.5
		18-35M	269	13	4.8	2.6	8.1	269	12	4.5	2.3	7.7
Overall/subject	Q-QIV	6-17M	157	18	11.5	6.9	17.5	157	18	11.5	6.9	17.5
		18-35M	142	19	13.4	8.3	20.1	142	18	12.7	7.7	19.3
	D-TIV-YB	6-17M	160	16	10.0	5.8	15.7	160	16	10.0	5.8	15.7
		18-35M	142	12	8.5	4.4	14.3	142	11	7.7	3.9	13.4

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	157	2	1.3	0.2	4.5
		18-35M	142	3	2.1	0.4	6.0
	D-TIV-YB	6-17M	160	1	0.6	0.0	3.4
		18-35M	142	0	0.0	0.0	2.6
Dose 2	Q-QIV	6-17M	155	2	1.3	0.2	4.6
		18-35M	122	1	0.8	0.0	4.5
	D-TIV-YB	6-17M	154	1	0.6	0.0	3.6
		18-35M	127	2	1.6	0.2	5.6
Overall/dose	Q-QIV	6-17M	312	4	1.3	0.4	3.2
		18-35M	264	4	1.5	0.4	3.8
	D-TIV-YB	6-17M	314	2	0.6	0.1	2.3
		18-35M	269	2	0.7	0.1	2.7
Overall/subject	Q-QIV	6-17M	157	4	2.5	0.7	6.4
		18-35M	142	3	2.1	0.4	6.0
	D-TIV-YB	6-17M	160	1	0.6	0.0	3.4
		18-35M	142	2	1.4	0.2	5.0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 132 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By age strata - Total Vaccinated cohort)

		Q-QIV										D-TIV-YB				
		6-17M					18-35M					6-17M				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Pain	All	154	25	16.2	10.8	23.0	136	48	35.3	27.3	43.9	156	19	12.2	7.5	18.4
	Grade 2 or 3	154	5	3.2	1.1	7.4	136	11	8.1	4.1	14.0	156	3	1.9	0.4	5.5
	Grade 3	154	2	1.3	0.2	4.6	136	3	2.2	0.5	6.3	156	1	0.6	0.0	3.5
	Medical advice	154	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
Redness (mm)	All	154	2	1.3	0.2	4.6	136	1	0.7	0.0	4.0	156	1	0.6	0.0	3.5
	>50.0	154	1	0.6	0.0	3.6	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	>100	154	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	Medical advice	154	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
Swelling (mm)	All	154	2	1.3	0.2	4.6	136	0	0.0	0.0	2.7	156	1	0.6	0.0	3.5
	>50.0	154	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	>100	154	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	Medical advice	154	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
Dose 2																
Pain	All	153	25	16.3	10.9	23.2	121	32	26.4	18.8	35.2	149	19	12.8	7.9	19.2
	Grade 2 or 3	153	8	5.2	2.3	10.0	121	10	8.3	4.0	14.7	149	2	1.3	0.2	4.8
	Grade 3	153	2	1.3	0.2	4.6	121	1	0.8	0.0	4.5	149	1	0.7	0.0	3.7
	Medical advice	153	1	0.7	0.0	3.6	121	0	0.0	0.0	3.0	149	0	0.0	0.0	2.4
Redness (mm)	All	153	3	2.0	0.4	5.6	121	1	0.8	0.0	4.5	149	2	1.3	0.2	4.8
	>50.0	153	1	0.7	0.0	3.6	121	0	0.0	0.0	3.0	149	0	0.0	0.0	2.4
	>100	153	0	0.0	0.0	2.4	121	0	0.0	0.0	3.0	149	0	0.0	0.0	2.4
	Medical advice	153	1	0.7	0.0	3.6	121	0	0.0	0.0	3.0	149	0	0.0	0.0	2.4
Swelling (mm)	All	153	4	2.6	0.7	6.6	121	0	0.0	0.0	3.0	149	2	1.3	0.2	4.8
	>50.0	153	1	0.7	0.0	3.6	121	0	0.0	0.0	3.0	149	0	0.0	0.0	2.4
	>100	153	0	0.0	0.0	2.4	121	0	0.0	0.0	3.0	149	0	0.0	0.0	2.4
	Medical advice	153	1	0.7	0.0	3.6	121	0	0.0	0.0	3.0	149	0	0.0	0.0	2.4
Overall/dose																
Pain	All	307	50	16.3	12.3	20.9	257	80	31.1	25.5	37.2	305	38	12.5	9.0	16.7
	Grade 2 or 3	307	13	4.2	2.3	7.1	257	21	8.2	5.1	12.2	305	5	1.6	0.5	3.8
	Grade 3	307	4	1.3	0.4	3.3	257	4	1.6	0.4	3.9	305	2	0.7	0.1	2.3
	Medical advice	307	1	0.3	0.0	1.8	257	0	0.0	0.0	1.4	305	0	0.0	0.0	1.2
Redness (mm)	All	307	5	1.6	0.5	3.8	257	2	0.8	0.1	2.8	305	3	1.0	0.2	2.8
	>50.0	307	2	0.7	0.1	2.3	257	0	0.0	0.0	1.4	305	0	0.0	0.0	1.2
	>100	307	0	0.0	0.0	1.2	257	0	0.0	0.0	1.4	305	0	0.0	0.0	1.2
	Medical advice	307	1	0.3	0.0	1.8	257	0	0.0	0.0	1.4	305	0	0.0	0.0	1.2
Swelling (mm)	All	307	6	2.0	0.7	4.2	257	0	0.0	0.0	1.4	305	3	1.0	0.2	2.8
	>50.0	307	1	0.3	0.0	1.8	257	0	0.0	0.0	1.4	305	0	0.0	0.0	1.2
	>100	307	0	0.0	0.0	1.2	257	0	0.0	0.0	1.4	305	0	0.0	0.0	1.2
	Medical advice	307	1	0.3	0.0	1.8	257	0	0.0	0.0	1.4	305	0	0.0	0.0	1.2
Overall/subject																
Pain	All	155	39	25.2	18.5	32.8	136	56	41.2	32.8	49.9	156	31	19.9	13.9	27.0
	Grade 2 or 3	155	11	7.1	3.6	12.3	136	16	11.8	6.9	18.4	156	4	2.6	0.7	6.4
	Grade 3	155	4	2.6	0.7	6.5	136	3	2.2	0.5	6.3	156	1	0.6	0.0	3.5
	Medical advice	155	1	0.6	0.0	3.5	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
Redness (mm)	All	155	4	2.6	0.7	6.5	136	2	1.5	0.2	5.2	156	3	1.9	0.4	5.5
	>50.0	155	2	1.3	0.2	4.6	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	>100	155	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	Medical advice	155	1	0.6	0.0	3.5	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3

		Q-QIV										D-TIV-YB				
		6-17M					18-35M					6-17M				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Swelling (mm)	All	155	5	3.2	1.1	7.4	136	0	0.0	0.0	2.7	156	2	1.3	0.2	4.6
	>50.0	155	1	0.6	0.0	3.5	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	>100	155	0	0.0	0.0	2.4	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3
	Medical advice	155	1	0.6	0.0	3.5	136	0	0.0	0.0	2.7	156	0	0.0	0.0	2.3

		D-TIV-YB					Total									
		18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1																
Pain	All	141	45	31.9	24.3	40.3	310	44	14.2	10.5	18.6	277	93	33.6	28.0	39.5
	Grade 2 or 3	141	4	2.8	0.8	7.1	310	8	2.6	1.1	5.0	277	15	5.4	3.1	8.8
	Grade 3	141	0	0.0	0.0	2.6	310	3	1.0	0.2	2.8	277	3	1.1	0.2	3.1
	Medical advice	141	0	0.0	0.0	2.6	310	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
Redness (mm)	All	141	1	0.7	0.0	3.9	310	3	1.0	0.2	2.8	277	2	0.7	0.1	2.6
	>50.0	141	0	0.0	0.0	2.6	310	1	0.3	0.0	1.8	277	0	0.0	0.0	1.3
	>100	141	0	0.0	0.0	2.6	310	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
	Medical advice	141	0	0.0	0.0	2.6	310	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
Swelling (mm)	All	141	1	0.7	0.0	3.9	310	3	1.0	0.2	2.8	277	1	0.4	0.0	2.0
	>50.0	141	0	0.0	0.0	2.6	310	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
	>100	141	0	0.0	0.0	2.6	310	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
	Medical advice	141	0	0.0	0.0	2.6	310	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
Dose 2																
Pain	All	127	40	31.5	23.5	40.3	302	44	14.6	10.8	19.1	248	72	29.0	23.5	35.1
	Grade 2 or 3	127	13	10.2	5.6	16.9	302	10	3.3	1.6	6.0	248	23	9.3	6.0	13.6
	Grade 3	127	2	1.6	0.2	5.6	302	3	1.0	0.2	2.9	248	3	1.2	0.3	3.5
	Medical advice	127	0	0.0	0.0	2.9	302	1	0.3	0.0	1.8	248	0	0.0	0.0	1.5
Redness (mm)	All	127	2	1.6	0.2	5.6	302	5	1.7	0.5	3.8	248	3	1.2	0.3	3.5
	>50.0	127	0	0.0	0.0	2.9	302	1	0.3	0.0	1.8	248	0	0.0	0.0	1.5
	>100	127	0	0.0	0.0	2.9	302	0	0.0	0.0	1.2	248	0	0.0	0.0	1.5
	Medical advice	127	0	0.0	0.0	2.9	302	1	0.3	0.0	1.8	248	0	0.0	0.0	1.5
Swelling (mm)	All	127	3	2.4	0.5	6.7	302	6	2.0	0.7	4.3	248	3	1.2	0.3	3.5
	>50.0	127	0	0.0	0.0	2.9	302	1	0.3	0.0	1.8	248	0	0.0	0.0	1.5
	>100	127	0	0.0	0.0	2.9	302	0	0.0	0.0	1.2	248	0	0.0	0.0	1.5
	Medical advice	127	0	0.0	0.0	2.9	302	1	0.3	0.0	1.8	248	0	0.0	0.0	1.5
Overall/dose																
Pain	All	268	85	31.7	26.2	37.7	612	88	14.4	11.7	17.4	525	165	31.4	27.5	35.6
	Grade 2 or 3	268	17	6.3	3.7	10.0	612	18	2.9	1.8	4.6	525	38	7.2	5.2	9.8
	Grade 3	268	2	0.7	0.1	2.7	612	6	1.0	0.4	2.1	525	6	1.1	0.4	2.5
	Medical advice	268	0	0.0	0.0	1.4	612	1	0.2	0.0	0.9	525	0	0.0	0.0	0.7
Redness (mm)	All	268	3	1.1	0.2	3.2	612	8	1.3	0.6	2.6	525	5	1.0	0.3	2.2
	>50.0	268	0	0.0	0.0	1.4	612	2	0.3	0.0	1.2	525	0	0.0	0.0	0.7
	>100	268	0	0.0	0.0	1.4	612	0	0.0	0.0	0.6	525	0	0.0	0.0	0.7
	Medical advice	268	0	0.0	0.0	1.4	612	1	0.2	0.0	0.9	525	0	0.0	0.0	0.7
Swelling (mm)	All	268	4	1.5	0.4	3.8	612	9	1.5	0.7	2.8	525	4	0.8	0.2	1.9
	>50.0	268	0	0.0	0.0	1.4	612	1	0.2	0.0	0.9	525	0	0.0	0.0	0.7
	>100	268	0	0.0	0.0	1.4	612	0	0.0	0.0	0.6	525	0	0.0	0.0	0.7
	Medical advice	268	0	0.0	0.0	1.4	612	1	0.2	0.0	0.9	525	0	0.0	0.0	0.7

		D-TIV-YB					Total									
		18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject																
Pain	All	141	60	42.6	34.3	51.2	311	70	22.5	18.0	27.6	277	116	41.9	36.0	47.9
	Grade 2 or 3	141	15	10.6	6.1	16.9	311	15	4.8	2.7	7.8	277	31	11.2	7.7	15.5
	Grade 3	141	2	1.4	0.2	5.0	311	5	1.6	0.5	3.7	277	5	1.8	0.6	4.2
	Medical advice	141	0	0.0	0.0	2.6	311	1	0.3	0.0	1.8	277	0	0.0	0.0	1.3
Redness (mm)	All	141	3	2.1	0.4	6.1	311	7	2.3	0.9	4.6	277	5	1.8	0.6	4.2
	>50.0	141	0	0.0	0.0	2.6	311	2	0.6	0.1	2.3	277	0	0.0	0.0	1.3
	>100	141	0	0.0	0.0	2.6	311	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
	Medical advice	141	0	0.0	0.0	2.6	311	1	0.3	0.0	1.8	277	0	0.0	0.0	1.3
Swelling (mm)	All	141	4	2.8	0.8	7.1	311	7	2.3	0.9	4.6	277	4	1.4	0.4	3.7
	>50.0	141	0	0.0	0.0	2.6	311	1	0.3	0.0	1.8	277	0	0.0	0.0	1.3
	>100	141	0	0.0	0.0	2.6	311	0	0.0	0.0	1.2	277	0	0.0	0.0	1.3
	Medical advice	141	0	0.0	0.0	2.6	311	1	0.3	0.0	1.8	277	0	0.0	0.0	1.3

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
Total : n/%= number/percentage of subjects/doses with at least one local symptom whatever the number of injections.
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 133 Incidence of solicited general symptoms (excluding fever) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By age strata - Total Vaccinated cohort)

		Q-QIV										D-TIV-YB				
		6-17M					18-35M					6-17M				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Drowsiness	All	154	40	26.0	19.2	33.6	135	32	23.7	16.8	31.8	155	39	25.2	18.5	32.8
	Grade 2 or 3	154	16	10.4	6.1	16.3	135	10	7.4	3.6	13.2	155	10	6.5	3.1	11.5
	Grade 3	154	2	1.3	0.2	4.6	135	4	3.0	0.8	7.4	155	3	1.9	0.4	5.6
	Related	154	31	20.1	14.1	27.3	135	28	20.7	14.2	28.6	155	33	21.3	15.1	28.6
	Grade 2 or 3 Related	154	11	7.1	3.6	12.4	135	10	7.4	3.6	13.2	155	8	5.2	2.3	9.9
	Grade 3 Related	154	1	0.6	0.0	3.6	135	4	3.0	0.8	7.4	155	2	1.3	0.2	4.6
	Medical advice	154	6	3.9	1.4	8.3	135	3	2.2	0.5	6.4	155	2	1.3	0.2	4.6
Irritability / fussiness	All	154	49	31.8	24.6	39.8	135	42	31.1	23.4	39.6	155	50	32.3	25.0	40.2
	Grade 2 or 3	154	20	13.0	8.1	19.3	135	15	11.1	6.4	17.7	155	19	12.3	7.5	18.5
	Grade 3	154	6	3.9	1.4	8.3	135	5	3.7	1.2	8.4	155	9	5.8	2.7	10.7
	Related	154	42	27.3	20.4	35.0	135	38	28.1	20.8	36.5	155	42	27.1	20.3	34.8
	Grade 2 or 3 Related	154	15	9.7	5.6	15.6	135	14	10.4	5.8	16.8	155	15	9.7	5.5	15.5
	Grade 3 Related	154	4	2.6	0.7	6.5	135	5	3.7	1.2	8.4	155	7	4.5	1.8	9.1
	Medical advice	154	5	3.2	1.1	7.4	135	5	3.7	1.2	8.4	155	4	2.6	0.7	6.5
Loss of appetite	All	154	38	24.7	18.1	32.3	135	40	29.6	22.1	38.1	155	33	21.3	15.1	28.6
	Grade 2 or 3	154	15	9.7	5.6	15.6	135	17	12.6	7.5	19.4	155	11	7.1	3.6	12.3
	Grade 3	154	2	1.3	0.2	4.6	135	7	5.2	2.1	10.4	155	4	2.6	0.7	6.5
	Related	154	33	21.4	15.2	28.8	135	34	25.2	18.1	33.4	155	26	16.8	11.3	23.6
	Grade 2 or 3 Related	154	11	7.1	3.6	12.4	135	16	11.9	6.9	18.5	155	7	4.5	1.8	9.1
	Grade 3 Related	154	2	1.3	0.2	4.6	135	7	5.2	2.1	10.4	155	1	0.6	0.0	3.5
	Medical advice	154	5	3.2	1.1	7.4	135	3	2.2	0.5	6.4	155	3	1.9	0.4	5.6
Dose 2																
Drowsiness	All	151	24	15.9	10.5	22.7	121	25	20.7	13.8	29.0	149	19	12.8	7.9	19.2
	Grade 2 or 3	151	8	5.3	2.3	10.2	121	7	5.8	2.4	11.6	149	4	2.7	0.7	6.7
	Grade 3	151	2	1.3	0.2	4.7	121	1	0.8	0.0	4.5	149	4	2.7	0.7	6.7
	Related	151	20	13.2	8.3	19.7	121	22	18.2	11.8	26.2	149	19	12.8	7.9	19.2
	Grade 2 or 3 Related	151	7	4.6	1.9	9.3	121	4	3.3	0.9	8.2	149	4	2.7	0.7	6.7
	Grade 3 Related	151	1	0.7	0.0	3.6	121	1	0.8	0.0	4.5	149	4	2.7	0.7	6.7
	Medical advice	151	3	2.0	0.4	5.7	121	3	2.5	0.5	7.1	149	1	0.7	0.0	3.7
Irritability / fussiness	All	151	37	24.5	17.9	32.2	121	35	28.9	21.0	37.9	149	39	26.2	19.3	34.0
	Grade 2 or 3	151	16	10.6	6.2	16.6	121	10	8.3	4.0	14.7	149	13	8.7	4.7	14.5
	Grade 3	151	3	2.0	0.4	5.7	121	3	2.5	0.5	7.1	149	4	2.7	0.7	6.7
	Related	151	33	21.9	15.5	29.3	121	30	24.8	17.4	33.5	149	36	24.2	17.5	31.8
	Grade 2 or 3 Related	151	16	10.6	6.2	16.6	121	6	5.0	1.8	10.5	149	10	6.7	3.3	12.0
	Grade 3 Related	151	3	2.0	0.4	5.7	121	1	0.8	0.0	4.5	149	3	2.0	0.4	5.8
	Medical advice	151	3	2.0	0.4	5.7	121	3	2.5	0.5	7.1	149	0	0.0	0.0	2.4
Loss of appetite	All	151	30	19.9	13.8	27.1	121	18	14.9	9.1	22.5	149	26	17.4	11.7	24.5
	Grade 2 or 3	151	11	7.3	3.7	12.7	121	9	7.4	3.5	13.7	149	9	6.0	2.8	11.2
	Grade 3	151	6	4.0	1.5	8.4	121	2	1.7	0.2	5.8	149	3	2.0	0.4	5.8
	Related	151	27	17.9	12.1	24.9	121	13	10.7	5.8	17.7	149	22	14.8	9.5	21.5
	Grade 2 or 3 Related	151	11	7.3	3.7	12.7	121	6	5.0	1.8	10.5	149	8	5.4	2.3	10.3

		Q-QIV										D-TIV-YB				
		6-17M					18-35M					6-17M				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3 Related	151	6	4.0	1.5	8.4	121	2	1.7	0.2	5.8	149	3	2.0	0.4	5.8
	Medical advice	151	4	2.6	0.7	6.6	121	4	3.3	0.9	8.2	149	1	0.7	0.0	3.7
Overall/dose																
Drowsiness	All	305	64	21.0	16.6	26.0	256	57	22.3	17.3	27.9	304	58	19.1	14.8	24.0
	Grade 2 or 3	305	24	7.9	5.1	11.5	256	17	6.6	3.9	10.4	304	14	4.6	2.5	7.6
	Grade 3	305	4	1.3	0.4	3.3	256	5	2.0	0.6	4.5	304	7	2.3	0.9	4.7
	Related	305	51	16.7	12.7	21.4	256	50	19.5	14.9	24.9	304	52	17.1	13.0	21.8
	Grade 2 or 3 Related	305	18	5.9	3.5	9.2	256	14	5.5	3.0	9.0	304	12	3.9	2.1	6.8
	Grade 3 Related	305	2	0.7	0.1	2.3	256	5	2.0	0.6	4.5	304	6	2.0	0.7	4.2
	Medical advice	305	9	3.0	1.4	5.5	256	6	2.3	0.9	5.0	304	3	1.0	0.2	2.9
Irritability / fussiness	All	305	86	28.2	23.2	33.6	256	77	30.1	24.5	36.1	304	89	29.3	24.2	34.7
	Grade 2 or 3	305	36	11.8	8.4	16.0	256	25	9.8	6.4	14.1	304	32	10.5	7.3	14.5
	Grade 3	305	9	3.0	1.4	5.5	256	8	3.1	1.4	6.1	304	13	4.3	2.3	7.2
	Related	305	75	24.6	19.9	29.8	256	68	26.6	21.3	32.4	304	78	25.7	20.8	31.0
	Grade 2 or 3 Related	305	31	10.2	7.0	14.1	256	20	7.8	4.8	11.8	304	25	8.2	5.4	11.9
	Grade 3 Related	305	7	2.3	0.9	4.7	256	6	2.3	0.9	5.0	304	10	3.3	1.6	6.0
	Medical advice	305	8	2.6	1.1	5.1	256	8	3.1	1.4	6.1	304	4	1.3	0.4	3.3
Loss of appetite	All	305	68	22.3	17.7	27.4	256	58	22.7	17.7	28.3	304	59	19.4	15.1	24.3
	Grade 2 or 3	305	26	8.5	5.6	12.2	256	26	10.2	6.7	14.5	304	20	6.6	4.1	10.0
	Grade 3	305	8	2.6	1.1	5.1	256	9	3.5	1.6	6.6	304	7	2.3	0.9	4.7
	Related	305	60	19.7	15.4	24.6	256	47	18.4	13.8	23.7	304	48	15.8	11.9	20.4
	Grade 2 or 3 Related	305	22	7.2	4.6	10.7	256	22	8.6	5.5	12.7	304	15	4.9	2.8	8.0
	Grade 3 Related	305	8	2.6	1.1	5.1	256	9	3.5	1.6	6.6	304	4	1.3	0.4	3.3
	Medical advice	305	9	3.0	1.4	5.5	256	7	2.7	1.1	5.6	304	4	1.3	0.4	3.3
Overall/subject																
Drowsiness	All	155	51	32.9	25.6	40.9	135	42	31.1	23.4	39.6	155	48	31.0	23.8	38.9
	Grade 2 or 3	155	20	12.9	8.1	19.2	135	14	10.4	5.8	16.8	155	13	8.4	4.5	13.9
	Grade 3	155	4	2.6	0.7	6.5	135	5	3.7	1.2	8.4	155	7	4.5	1.8	9.1
	Related	155	43	27.7	20.9	35.5	135	36	26.7	19.4	35.0	155	44	28.4	21.4	36.2
	Grade 2 or 3 Related	155	16	10.3	6.0	16.2	135	12	8.9	4.7	15.0	155	11	7.1	3.6	12.3
	Grade 3 Related	155	2	1.3	0.2	4.6	135	5	3.7	1.2	8.4	155	6	3.9	1.4	8.2
	Medical advice	155	7	4.5	1.8	9.1	135	6	4.4	1.6	9.4	155	3	1.9	0.4	5.6
Irritability / fussiness	All	155	63	40.6	32.8	48.8	135	55	40.7	32.4	49.5	155	66	42.6	34.7	50.8
	Grade 2 or 3	155	31	20.0	14.0	27.2	135	23	17.0	11.1	24.5	155	28	18.1	12.4	25.0
	Grade 3	155	8	5.2	2.3	9.9	135	7	5.2	2.1	10.4	155	12	7.7	4.1	13.1
	Related	155	56	36.1	28.6	44.2	135	48	35.6	27.5	44.2	155	60	38.7	31.0	46.9
	Grade 2 or 3 Related	155	26	16.8	11.3	23.6	135	20	14.8	9.3	21.9	155	21	13.5	8.6	20.0
	Grade 3 Related	155	6	3.9	1.4	8.2	135	6	4.4	1.6	9.4	155	9	5.8	2.7	10.7
	Medical advice	155	6	3.9	1.4	8.2	135	8	5.9	2.6	11.3	155	4	2.6	0.7	6.5
Loss of appetite	All	155	52	33.5	26.2	41.6	135	47	34.8	26.8	43.5	155	46	29.7	22.6	37.5
	Grade 2 or 3	155	21	13.5	8.6	20.0	135	22	16.3	10.5	23.6	155	18	11.6	7.0	17.7
	Grade 3	155	8	5.2	2.3	9.9	135	8	5.9	2.6	11.3	155	7	4.5	1.8	9.1
	Related	155	46	29.7	22.6	37.5	135	38	28.1	20.8	36.5	155	38	24.5	18.0	32.1
	Grade 2 or 3 Related	155	18	11.6	7.0	17.7	135	19	14.1	8.7	21.1	155	14	9.0	5.0	14.7
	Grade 3 Related	155	8	5.2	2.3	9.9	135	8	5.9	2.6	11.3	155	4	2.6	0.7	6.5
	Medical advice	155	7	4.5	1.8	9.1	135	7	5.2	2.1	10.4	155	4	2.6	0.7	6.5

		D-TIV-YB					Total									
		18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1																
Drowsiness	All	141	25	17.7	11.8	25.1	309	79	25.6	20.8	30.8	276	57	20.7	16.0	25.9
	Grade 2 or 3	141	8	5.7	2.5	10.9	309	26	8.4	5.6	12.1	276	18	6.5	3.9	10.1
	Grade 3	141	1	0.7	0.0	3.9	309	5	1.6	0.5	3.7	276	5	1.8	0.6	4.2
	Related	141	22	15.6	10.0	22.7	309	64	20.7	16.3	25.7	276	50	18.1	13.8	23.2
	Grade 2 or 3 Related	141	8	5.7	2.5	10.9	309	19	6.1	3.7	9.4	276	18	6.5	3.9	10.1
	Grade 3 Related	141	1	0.7	0.0	3.9	309	3	1.0	0.2	2.8	276	5	1.8	0.6	4.2
	Medical advice	141	0	0.0	0.0	2.6	309	8	2.6	1.1	5.0	276	3	1.1	0.2	3.1
Irritability / fussiness	All	141	44	31.2	23.7	39.5	309	99	32.0	26.9	37.6	276	86	31.2	25.7	37.0
	Grade 2 or 3	141	12	8.5	4.5	14.4	309	39	12.6	9.1	16.8	276	27	9.8	6.5	13.9
	Grade 3	141	1	0.7	0.0	3.9	309	15	4.9	2.7	7.9	276	6	2.2	0.8	4.7
	Related	141	34	24.1	17.3	32.0	309	84	27.2	22.3	32.5	276	72	26.1	21.0	31.7
	Grade 2 or 3 Related	141	9	6.4	3.0	11.8	309	30	9.7	6.6	13.6	276	23	8.3	5.4	12.2
	Grade 3 Related	141	1	0.7	0.0	3.9	309	11	3.6	1.8	6.3	276	6	2.2	0.8	4.7
	Medical advice	141	2	1.4	0.2	5.0	309	9	2.9	1.3	5.5	276	7	2.5	1.0	5.2
Loss of appetite	All	141	38	27.0	19.8	35.1	309	71	23.0	18.4	28.1	276	78	28.3	23.0	34.0
	Grade 2 or 3	141	10	7.1	3.5	12.7	309	26	8.4	5.6	12.1	276	27	9.8	6.5	13.9
	Grade 3	141	3	2.1	0.4	6.1	309	6	1.9	0.7	4.2	276	10	3.6	1.8	6.6
	Related	141	31	22.0	15.5	29.7	309	59	19.1	14.9	23.9	276	65	23.6	18.7	29.0
	Grade 2 or 3 Related	141	8	5.7	2.5	10.9	309	18	5.8	3.5	9.1	276	24	8.7	5.7	12.7
	Grade 3 Related	141	2	1.4	0.2	5.0	309	3	1.0	0.2	2.8	276	9	3.3	1.5	6.1
	Medical advice	141	2	1.4	0.2	5.0	309	8	2.6	1.1	5.0	276	5	1.8	0.6	4.2
Dose 2																
Drowsiness	All	127	25	19.7	13.2	27.7	300	43	14.3	10.6	18.8	248	50	20.2	15.4	25.7
	Grade 2 or 3	127	9	7.1	3.3	13.0	300	12	4.0	2.1	6.9	248	16	6.5	3.7	10.3
	Grade 3	127	1	0.8	0.0	4.3	300	6	2.0	0.7	4.3	248	2	0.8	0.1	2.9
	Related	127	23	18.1	11.8	25.9	300	39	13.0	9.4	17.3	248	45	18.1	13.6	23.5
	Grade 2 or 3 Related	127	8	6.3	2.8	12.0	300	11	3.7	1.8	6.5	248	12	4.8	2.5	8.3
	Grade 3 Related	127	1	0.8	0.0	4.3	300	5	1.7	0.5	3.8	248	2	0.8	0.1	2.9
	Medical advice	127	0	0.0	0.0	2.9	300	4	1.3	0.4	3.4	248	3	1.2	0.3	3.5
Irritability / fussiness	All	127	36	28.3	20.7	37.0	300	76	25.3	20.5	30.7	248	71	28.6	23.1	34.7
	Grade 2 or 3	127	15	11.8	6.8	18.7	300	29	9.7	6.6	13.6	248	25	10.1	6.6	14.5
	Grade 3	127	1	0.8	0.0	4.3	300	7	2.3	0.9	4.7	248	4	1.6	0.4	4.1
	Related	127	31	24.4	17.2	32.8	300	69	23.0	18.4	28.2	248	61	24.6	19.4	30.4
	Grade 2 or 3 Related	127	13	10.2	5.6	16.9	300	26	8.7	5.7	12.4	248	19	7.7	4.7	11.7
	Grade 3 Related	127	1	0.8	0.0	4.3	300	6	2.0	0.7	4.3	248	2	0.8	0.1	2.9
	Medical advice	127	1	0.8	0.0	4.3	300	3	1.0	0.2	2.9	248	4	1.6	0.4	4.1
Loss of appetite	All	127	29	22.8	15.9	31.1	300	56	18.7	14.4	23.5	248	47	19.0	14.3	24.4
	Grade 2 or 3	127	9	7.1	3.3	13.0	300	20	6.7	4.1	10.1	248	18	7.3	4.4	11.2
	Grade 3	127	5	3.9	1.3	8.9	300	9	3.0	1.4	5.6	248	7	2.8	1.1	5.7
	Related	127	24	18.9	12.5	26.8	300	49	16.3	12.3	21.0	248	37	14.9	10.7	20.0
	Grade 2 or 3 Related	127	8	6.3	2.8	12.0	300	19	6.3	3.9	9.7	248	14	5.6	3.1	9.3
	Grade 3 Related	127	5	3.9	1.3	8.9	300	9	3.0	1.4	5.6	248	7	2.8	1.1	5.7
	Medical advice	127	2	1.6	0.2	5.6	300	5	1.7	0.5	3.8	248	6	2.4	0.9	5.2

		D-TIV-YB					Total									
		18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/dose																
Drowsiness	All	268	50	18.7	14.2	23.8	609	122	20.0	16.9	23.4	524	107	20.4	17.0	24.1
	Grade 2 or 3	268	17	6.3	3.7	10.0	609	38	6.2	4.5	8.5	524	34	6.5	4.5	8.9
	Grade 3	268	2	0.7	0.1	2.7	609	11	1.8	0.9	3.2	524	7	1.3	0.5	2.7
	Related	268	45	16.8	12.5	21.8	609	103	16.9	14.0	20.1	524	95	18.1	14.9	21.7
	Grade 2 or 3 Related	268	16	6.0	3.5	9.5	609	30	4.9	3.3	7.0	524	30	5.7	3.9	8.1
	Grade 3 Related	268	2	0.7	0.1	2.7	609	8	1.3	0.6	2.6	524	7	1.3	0.5	2.7
	Medical advice	268	0	0.0	0.0	1.4	609	12	2.0	1.0	3.4	524	6	1.1	0.4	2.5
Irritability / fussiness	All	268	80	29.9	24.4	35.7	609	175	28.7	25.2	32.5	524	157	30.0	26.1	34.1
	Grade 2 or 3	268	27	10.1	6.7	14.3	609	68	11.2	8.8	13.9	524	52	9.9	7.5	12.8
	Grade 3	268	2	0.7	0.1	2.7	609	22	3.6	2.3	5.4	524	10	1.9	0.9	3.5
	Related	268	65	24.3	19.2	29.8	609	153	25.1	21.7	28.8	524	133	25.4	21.7	29.3
	Grade 2 or 3 Related	268	22	8.2	5.2	12.2	609	56	9.2	7.0	11.8	524	42	8.0	5.8	10.7
	Grade 3 Related	268	2	0.7	0.1	2.7	609	17	2.8	1.6	4.4	524	8	1.5	0.7	3.0
	Medical advice	268	3	1.1	0.2	3.2	609	12	2.0	1.0	3.4	524	11	2.1	1.1	3.7
Loss of appetite	All	268	67	25.0	19.9	30.6	609	127	20.9	17.7	24.3	524	125	23.9	20.3	27.7
	Grade 2 or 3	268	19	7.1	4.3	10.8	609	46	7.6	5.6	9.9	524	45	8.6	6.3	11.3
	Grade 3	268	8	3.0	1.3	5.8	609	15	2.5	1.4	4.0	524	17	3.2	1.9	5.1
	Related	268	55	20.5	15.9	25.9	609	108	17.7	14.8	21.0	524	102	19.5	16.2	23.1
	Grade 2 or 3 Related	268	16	6.0	3.5	9.5	609	37	6.1	4.3	8.3	524	38	7.3	5.2	9.8
	Grade 3 Related	268	7	2.6	1.1	5.3	609	12	2.0	1.0	3.4	524	16	3.1	1.8	4.9
	Medical advice	268	4	1.5	0.4	3.8	609	13	2.1	1.1	3.6	524	11	2.1	1.1	3.7
Overall/subject																
Drowsiness	All	141	40	28.4	21.1	36.6	310	99	31.9	26.8	37.4	276	82	29.7	24.4	35.5
	Grade 2 or 3	141	14	9.9	5.5	16.1	310	33	10.6	7.4	14.6	276	28	10.1	6.8	14.3
	Grade 3	141	2	1.4	0.2	5.0	310	11	3.5	1.8	6.3	276	7	2.5	1.0	5.2
	Related	141	36	25.5	18.6	33.6	310	87	28.1	23.1	33.4	276	72	26.1	21.0	31.7
	Grade 2 or 3 Related	141	13	9.2	5.0	15.3	310	27	8.7	5.8	12.4	276	25	9.1	5.9	13.1
	Grade 3 Related	141	2	1.4	0.2	5.0	310	8	2.6	1.1	5.0	276	7	2.5	1.0	5.2
	Medical advice	141	0	0.0	0.0	2.6	310	10	3.2	1.6	5.9	276	6	2.2	0.8	4.7
Irritability / fussiness	All	141	57	40.4	32.3	49.0	310	129	41.6	36.1	47.3	276	112	40.6	34.7	46.6
	Grade 2 or 3	141	23	16.3	10.6	23.5	310	59	19.0	14.8	23.9	276	46	16.7	12.5	21.6
	Grade 3	141	2	1.4	0.2	5.0	310	20	6.5	4.0	9.8	276	9	3.3	1.5	6.1
	Related	141	46	32.6	25.0	41.0	310	116	37.4	32.0	43.1	276	94	34.1	28.5	40.0
	Grade 2 or 3 Related	141	18	12.8	7.7	19.4	310	47	15.2	11.4	19.6	276	38	13.8	9.9	18.4
	Grade 3 Related	141	2	1.4	0.2	5.0	310	15	4.8	2.7	7.9	276	8	2.9	1.3	5.6
	Medical advice	141	3	2.1	0.4	6.1	310	10	3.2	1.6	5.9	276	11	4.0	2.0	7.0
Loss of appetite	All	141	54	38.3	30.2	46.9	310	98	31.6	26.5	37.1	276	101	36.6	30.9	42.6
	Grade 2 or 3	141	15	10.6	6.1	16.9	310	39	12.6	9.1	16.8	276	37	13.4	9.6	18.0
	Grade 3	141	7	5.0	2.0	10.0	310	15	4.8	2.7	7.9	276	15	5.4	3.1	8.8
	Related	141	45	31.9	24.3	40.3	310	84	27.1	22.2	32.4	276	83	30.1	24.7	35.9
	Grade 2 or 3 Related	141	13	9.2	5.0	15.3	310	32	10.3	7.2	14.3	276	32	11.6	8.1	16.0
	Grade 3 Related	141	7	5.0	2.0	10.0	310	12	3.9	2.0	6.7	276	15	5.4	3.1	8.8
	Medical advice	141	4	2.8	0.8	7.1	310	11	3.5	1.8	6.3	276	11	4.0	2.0	7.0

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
For each dose and overall/subject:
N= number of subjects with at least one documented dose; n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses; n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper lim

Table 134 Incidence of solicited symptoms (Fever) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By age strata - Total Vaccinated cohort)

		Q-QIV										D-TIV-YB				
		6-17M					18-35M					6-17M				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Temperature/(Axillary) (°C)	All	154	20	13.0	8.1	19.3	135	24	17.8	11.7	25.3	155	28	18.1	12.4	25.0
	≥38	154	19	12.3	7.6	18.6	135	23	17.0	11.1	24.5	155	27	17.4	11.8	24.3
	≥38.5	154	8	5.2	2.3	10.0	135	13	9.6	5.2	15.9	155	11	7.1	3.6	12.3
	≥39.0	154	3	1.9	0.4	5.6	135	8	5.9	2.6	11.3	155	6	3.9	1.4	8.2
	≥40.0	154	1	0.6	0.0	3.6	135	0	0.0	0.0	2.7	155	2	1.3	0.2	4.6
	Related	154	14	9.1	5.1	14.8	135	19	14.1	8.7	21.1	155	21	13.5	8.6	20.0
	≥38 Related	154	13	8.4	4.6	14.0	135	18	13.3	8.1	20.3	155	20	12.9	8.1	19.2
	≥38.5 Related	154	5	3.2	1.1	7.4	135	12	8.9	4.7	15.0	155	6	3.9	1.4	8.2
	≥39.0 Related	154	1	0.6	0.0	3.6	135	7	5.2	2.1	10.4	155	2	1.3	0.2	4.6
	≥40.0 Related	154	1	0.6	0.0	3.6	135	0	0.0	0.0	2.7	155	1	0.6	0.0	3.5
Dose 2																
Temperature/(Axillary) (°C)	All	151	19	12.6	7.7	19.0	121	12	9.9	5.2	16.7	149	15	10.1	5.7	16.1
	≥38	151	18	11.9	7.2	18.2	121	10	8.3	4.0	14.7	149	15	10.1	5.7	16.1
	≥38.5	151	14	9.3	5.2	15.1	121	8	6.6	2.9	12.6	149	11	7.4	3.7	12.8
	≥39.0	151	8	5.3	2.3	10.2	121	4	3.3	0.9	8.2	149	5	3.4	1.1	7.7
	≥40.0	151	0	0.0	0.0	2.4	121	2	1.7	0.2	5.8	149	1	0.7	0.0	3.7
	Related	151	15	9.9	5.7	15.9	121	9	7.4	3.5	13.7	149	13	8.7	4.7	14.5
	≥38 Related	151	15	9.9	5.7	15.9	121	7	5.8	2.4	11.6	149	13	8.7	4.7	14.5
	≥38.5 Related	151	12	7.9	4.2	13.5	121	6	5.0	1.8	10.5	149	9	6.0	2.8	11.2
	≥39.0 Related	151	6	4.0	1.5	8.4	121	3	2.5	0.5	7.1	149	4	2.7	0.7	6.7
	≥40.0 Related	151	0	0.0	0.0	2.4	121	1	0.8	0.0	4.5	149	1	0.7	0.0	3.7
Overall/dose																
Temperature/(Axillary) (°C)	All	305	39	12.8	9.3	17.1	256	36	14.1	10.0	18.9	304	43	14.1	10.4	18.6
	≥38	305	37	12.1	8.7	16.3	256	33	12.9	9.0	17.6	304	42	13.8	10.1	18.2
	≥38.5	305	22	7.2	4.6	10.7	256	21	8.2	5.1	12.3	304	22	7.2	4.6	10.8
	≥39.0	305	11	3.6	1.8	6.4	256	12	4.7	2.4	8.0	304	11	3.6	1.8	6.4
	≥40.0	305	1	0.3	0.0	1.8	256	2	0.8	0.1	2.8	304	3	1.0	0.2	2.9
	Related	305	29	9.5	6.5	13.4	256	28	10.9	7.4	15.4	304	34	11.2	7.9	15.3
	≥38 Related	305	28	9.2	6.2	13.0	256	25	9.8	6.4	14.1	304	33	10.9	7.6	14.9
	≥38.5 Related	305	17	5.6	3.3	8.8	256	18	7.0	4.2	10.9	304	15	4.9	2.8	8.0
	≥39.0 Related	305	7	2.3	0.9	4.7	256	10	3.9	1.9	7.1	304	6	2.0	0.7	4.2
	≥40.0 Related	305	1	0.3	0.0	1.8	256	1	0.4	0.0	2.2	304	2	0.7	0.1	2.4
Overall/subject																
Temperature/(Axillary) (°C)	All	155	32	20.6	14.6	27.9	135	34	25.2	18.1	33.4	155	38	24.5	18.0	32.1
	≥38	155	30	19.4	13.5	26.5	135	31	23.0	16.2	31.0	155	37	23.9	17.4	31.4
	≥38.5	155	21	13.5	8.6	20.0	135	19	14.1	8.7	21.1	155	21	13.5	8.6	20.0
	≥39.0	155	11	7.1	3.6	12.3	135	12	8.9	4.7	15.0	155	10	6.5	3.1	11.5
	≥40.0	155	1	0.6	0.0	3.5	135	2	1.5	0.2	5.2	155	3	1.9	0.4	5.6
	Related	155	23	14.8	9.6	21.4	135	26	19.3	13.0	26.9	155	30	19.4	13.5	26.5
	≥38 Related	155	22	14.2	9.1	20.7	135	23	17.0	11.1	24.5	155	29	18.7	12.9	25.8
	≥38.5 Related	155	16	10.3	6.0	16.2	135	16	11.9	6.9	18.5	155	15	9.7	5.5	15.5
	≥39.0 Related	155	7	4.5	1.8	9.1	135	10	7.4	3.6	13.2	155	6	3.9	1.4	8.2
	≥40.0 Related	155	1	0.6	0.0	3.5	135	1	0.7	0.0	4.1	155	2	1.3	0.2	4.6

		D-TIV-YB					Total									
		18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1																
Temperature/(Axillary) (°C)	All	141	16	11.3	6.6	17.8	309	48	15.5	11.7	20.1	276	40	14.5	10.6	19.2
	≥38	141	16	11.3	6.6	17.8	309	46	14.9	11.1	19.4	276	39	14.1	10.2	18.8
	≥38.5	141	11	7.8	4.0	13.5	309	19	6.1	3.7	9.4	276	24	8.7	5.7	12.7
	≥39.0	141	3	2.1	0.4	6.1	309	9	2.9	1.3	5.5	276	11	4.0	2.0	7.0
	≥40.0	141	0	0.0	0.0	2.6	309	3	1.0	0.2	2.8	276	0	0.0	0.0	1.3
	Related	141	10	7.1	3.5	12.7	309	35	11.3	8.0	15.4	276	29	10.5	7.2	14.7
	≥38 Related	141	10	7.1	3.5	12.7	309	33	10.7	7.5	14.7	276	28	10.1	6.8	14.3
	≥38.5 Related	141	7	5.0	2.0	10.0	309	11	3.6	1.8	6.3	276	19	6.9	4.2	10.5
	≥39.0 Related	141	3	2.1	0.4	6.1	309	3	1.0	0.2	2.8	276	10	3.6	1.8	6.6
	≥40.0 Related	141	0	0.0	0.0	2.6	309	2	0.6	0.1	2.3	276	0	0.0	0.0	1.3
Dose 2																
Temperature/(Axillary) (°C)	All	127	10	7.9	3.8	14.0	300	34	11.3	8.0	15.5	248	22	8.9	5.6	13.1
	≥38	127	10	7.9	3.8	14.0	300	33	11.0	7.7	15.1	248	20	8.1	5.0	12.2
	≥38.5	127	2	1.6	0.2	5.6	300	25	8.3	5.5	12.1	248	10	4.0	2.0	7.3
	≥39.0	127	0	0.0	0.0	2.9	300	13	4.3	2.3	7.3	248	4	1.6	0.4	4.1
	≥40.0	127	0	0.0	0.0	2.9	300	1	0.3	0.0	1.8	248	2	0.8	0.1	2.9
	Related	127	8	6.3	2.8	12.0	300	28	9.3	6.3	13.2	248	17	6.9	4.0	10.7
	≥38 Related	127	8	6.3	2.8	12.0	300	28	9.3	6.3	13.2	248	15	6.0	3.4	9.8
	≥38.5 Related	127	1	0.8	0.0	4.3	300	21	7.0	4.4	10.5	248	7	2.8	1.1	5.7
	≥39.0 Related	127	0	0.0	0.0	2.9	300	10	3.3	1.6	6.0	248	3	1.2	0.3	3.5
	≥40.0 Related	127	0	0.0	0.0	2.9	300	1	0.3	0.0	1.8	248	1	0.4	0.0	2.2
Overall/dose																
Temperature/(Axillary) (°C)	All	268	26	9.7	6.4	13.9	609	82	13.5	10.9	16.4	524	62	11.8	9.2	14.9
	≥38	268	26	9.7	6.4	13.9	609	79	13.0	10.4	15.9	524	59	11.3	8.7	14.3
	≥38.5	268	13	4.9	2.6	8.2	609	44	7.2	5.3	9.6	524	34	6.5	4.5	8.9
	≥39.0	268	3	1.1	0.2	3.2	609	22	3.6	2.3	5.4	524	15	2.9	1.6	4.7
	≥40.0	268	0	0.0	0.0	1.4	609	4	0.7	0.2	1.7	524	2	0.4	0.0	1.4
	Related	268	18	6.7	4.0	10.4	609	63	10.3	8.0	13.0	524	46	8.8	6.5	11.5
	≥38 Related	268	18	6.7	4.0	10.4	609	61	10.0	7.7	12.7	524	43	8.2	6.0	10.9
	≥38.5 Related	268	8	3.0	1.3	5.8	609	32	5.3	3.6	7.3	524	26	5.0	3.3	7.2
	≥39.0 Related	268	3	1.1	0.2	3.2	609	13	2.1	1.1	3.6	524	13	2.5	1.3	4.2
	≥40.0 Related	268	0	0.0	0.0	1.4	609	3	0.5	0.1	1.4	524	1	0.2	0.0	1.1
Overall/subject																
Temperature/(Axillary) (°C)	All	141	23	16.3	10.6	23.5	310	70	22.6	18.0	27.6	276	57	20.7	16.0	25.9
	≥38	141	23	16.3	10.6	23.5	310	67	21.6	17.2	26.6	276	54	19.6	15.1	24.7
	≥38.5	141	12	8.5	4.5	14.4	310	42	13.5	9.9	17.9	276	31	11.2	7.8	15.6
	≥39.0	141	3	2.1	0.4	6.1	310	21	6.8	4.2	10.2	276	15	5.4	3.1	8.8
	≥40.0	141	0	0.0	0.0	2.6	310	4	1.3	0.4	3.3	276	2	0.7	0.1	2.6
	Related	141	18	12.8	7.7	19.4	310	53	17.1	13.1	21.8	276	44	15.9	11.8	20.8
	≥38 Related	141	18	12.8	7.7	19.4	310	51	16.5	12.5	21.1	276	41	14.9	10.9	19.6
	≥38.5 Related	141	8	5.7	2.5	10.9	310	31	10.0	6.9	13.9	276	24	8.7	5.7	12.7
	≥39.0 Related	141	3	2.1	0.4	6.1	310	13	4.2	2.3	7.1	276	13	4.7	2.5	7.9
	≥40.0 Related	141	0	0.0	0.0	2.6	310	3	1.0	0.2	2.8	276	1	0.4	0.0	2.0

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
For each dose and overall/subject: N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses; n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 135 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		74	47.1	39.1	55.2	68	47.9	39.4	56.4	93	58.1	50.1	65.9	72	50.7	42.2	59.2
---------- ( )	---------- ( )	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1*	0.6	0.0	3.4	1**	0.7	0.0	3.9
Ear and labyrinth disorders (10013993)	Ear haemorrhage (10014009)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Ear pain (10014020)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Eye disorders (10015919)	Conjunctivitis (10010741)	2	1.3	0.2	4.5	1	0.7	0.0	3.9	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Lacrimation increased (10023644)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Diarrhoea (10012735)	19	12.1	7.4	18.3	19	13.4	8.3	20.1	23	14.4	9.3	20.8	15	10.6	6.0	16.8
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Enteritis (10014866)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Faeces hard (10016101)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Flatulence (10016766)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	1	0.7	0.0	3.9
	Stomatitis (10042128)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Teething (10043183)	8	5.1	2.2	9.8	1	0.7	0.0	3.9	4	2.5	0.7	6.3	3	2.1	0.4	6.0
	Vomiting (10047700)	5	3.2	1.0	7.3	2	1.4	0.2	5.0	5	3.1	1.0	7.1	2	1.4	0.2	5.0
General disorders and administration site conditions (10018065)	Injection site erosion (10022059)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Injection site haematoma (10022066)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Injection site rash (10022094)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Irritability (10022998)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	3	1.9	0.4	5.4	1	0.7	0.0	3.9
	Pyrexia (10037660)	5	3.2	1.0	7.3	1	0.7	0.0	3.9	6	3.8	1.4	8.0	4	2.8	0.8	7.1
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Acute sinusitis (10001076)	3	1.9	0.4	5.5	1	0.7	0.0	3.9	2	1.3	0.2	4.4	1	0.7	0.0	3.9
	Acute tonsillitis (10001093)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Ascariasis (10003442)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Blastocystis infection (10005092)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Bronchiolitis (10006448)	4	2.5	0.7	6.4	0	0.0	0.0	2.6	4	2.5	0.7	6.3	0	0.0	0.0	2.6
	Bronchitis (10006451)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	2	1.3	0.2	4.4	0	0.0	0.0	2.6
	Bronchopneumonia (10006469)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Bullous impetigo (10006563)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Cellulitis (10007882)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	2	1.3	0.2	4.4	1	0.7	0.0	3.9
	Croup infectious (10011416)	0	0.0	0.0	2.3	2	1.4	0.2	5.0	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Cutaneous larva migrans (10059547)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Dengue fever (10012310)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Dysentery (10051402)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	2	1.3	0.2	4.4	0	0.0	0.0	2.6
	Ear infection (10014011)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	5	3.1	1.0	7.1	1	0.7	0.0	3.9
	Gastroenteritis (10017888)	8	5.1	2.2	9.8	4	2.8	0.8	7.1	4	2.5	0.7	6.3	3	2.1	0.4	6.0
	Gingivitis (10018292)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Impetigo (10021531)	1	0.6	0.0	3.5	2	1.4	0.2	5.0	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Infection parasitic (10021857)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Injection site cellulitis (10050057)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Laryngitis (10023874)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Lung infection (10061229)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Nasopharyngitis (10028810)	42	26.8	20.0	34.4	36	25.4	18.4	33.3	47	29.4	22.4	37.1	43	30.3	22.9	38.5
	Otitis media (10033078)	0	0.0	0.0	2.3	3	2.1	0.4	6.0	4	2.5	0.7	6.3	1	0.7	0.0	3.9
	Otitis media acute (10033079)	2	1.3	0.2	4.5	1	0.7	0.0	3.9	3	1.9	0.4	5.4	0	0.0	0.0	2.6
	Parasitic gastroenteritis (10067720)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	1	0.6	0.0	3.4	1	0.7	0.0	3.9
	Pharyngitis (10034835)	5	3.2	1.0	7.3	6	4.2	1.6	9.0	4	2.5	0.7	6.3	3	2.1	0.4	6.0
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Pneumonia (10035664)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Rhinitis (10039083)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	4	2.5	0.7	6.3	0	0.0	0.0	2.6
	Roseola (10039222)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Scarlet fever (10039587)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Sinusitis (10040753)	2	1.3	0.2	4.5	3	2.1	0.4	6.0	3	1.9	0.4	5.4	1	0.7	0.0	3.9

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Subcutaneous abscess (10042343)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Tinea pedis (10043873)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Tonsillitis (10044008)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	3	1.9	0.4	5.4	0	0.0	0.0	2.6
	Tooth abscess (10044016)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Upper respiratory tract infection (10046306)	4	2.5	0.7	6.4	3	2.1	0.4	6.0	6	3.8	1.4	8.0	4	2.8	0.8	7.1
	Viral infection (10047461)	2	1.3	0.2	4.5	2	1.4	0.2	5.0	1	0.6	0.0	3.4	1	0.7	0.0	3.9
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Face injury (10050392)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Joint injury (10060820)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Lethargy (10024264)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	1	0.7	0.0	3.9
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	2	1.4	0.2	5.0
	Bronchial hyperreactivity (10066091)	1	0.6	0.0	3.5	4	2.8	0.8	7.1	2	1.3	0.2	4.4	3	2.1	0.4	6.0
	Cough (10011224)	6	3.8	1.4	8.1	7	4.9	2.0	9.9	2	1.3	0.2	4.4	3	2.1	0.4	6.0
	Nasal congestion (10028735)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Rhinitis allergic (10039085)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Rhinorrhoea (10039101)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	2	1.3	0.2	4.4	2	1.4	0.2	5.0
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	0	0.0	0.0	2.3	2	1.4	0.2	5.0	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Dermatitis (10012431)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Dermatitis contact (10012442)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Dermatitis diaper (10012444)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Dermatosis (10048768)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	2	1.4	0.2	5.0
	Dry skin (10013786)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Ecchymosis (10014080)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Eczema (10014184)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	3	1.9	0.4	5.4	0	0.0	0.0	2.6
	Erythema (10015150)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	2	1.3	0.2	4.4	1	0.7	0.0	3.9

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Onychoclasis (10048886)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Prurigo (10037083)	2	1.3	0.2	4.5	1	0.7	0.0	3.9	2	1.3	0.2	4.4	0	0.0	0.0	2.6
	Rash (10037844)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	1	0.6	0.0	3.4	3	2.1	0.4	6.0
	Rash generalised (10037858)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Swelling face (10042682)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Urticaria (10046735)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	1	0.6	0.0	3.4	1	0.7	0.0	3.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "FEVER" which was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.
**Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 136 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		103	33.0	27.8	38.5	90	34.1	28.4	40.2	120	38.2	32.8	43.8	89	33.1	27.5	39.1
---------- ( )	---------- ( )	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1*	0.3	0.0	1.8	1**	0.4	0.0	2.1
Ear and labyrinth disorders (10013993)	Ear haemorrhage (10014009)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Ear pain (10014020)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Eye disorders (10015919)	Conjunctivitis (10010741)	2	0.6	0.1	2.3	1	0.4	0.0	2.1	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Lacrimation increased (10023644)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Diarrhoea (10012735)	23	7.4	4.7	10.9	20	7.6	4.7	11.5	25	8.0	5.2	11.5	17	6.3	3.7	9.9
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Enteritis (10014866)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Faeces hard (10016101)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Flatulence (10016766)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	1	0.4	0.0	2.1
	Stomatitis (10042128)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Teething (10043183)	10	3.2	1.5	5.8	2	0.8	0.1	2.7	5	1.6	0.5	3.7	3	1.1	0.2	3.2
	Vomiting (10047700)	6	1.9	0.7	4.1	2	0.8	0.1	2.7	5	1.6	0.5	3.7	2	0.7	0.1	2.7
General disorders and administration site conditions (10018065)	Injection site erosion (10022059)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Injection site haematoma (10022066)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Injection site rash (10022094)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Irritability (10022998)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	3	1.0	0.2	2.8	1	0.4	0.0	2.1
	Pyrexia (10037660)	5	1.6	0.5	3.7	1	0.4	0.0	2.1	7	2.2	0.9	4.5	4	1.5	0.4	3.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Acute sinusitis (10001076)	3	1.0	0.2	2.8	1	0.4	0.0	2.1	2	0.6	0.1	2.3	1	0.4	0.0	2.1
	Acute tonsillitis (10001093)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Ascariasis (10003442)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Blastocystis infection (10005092)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Bronchiolitis (10006448)	4	1.3	0.4	3.2	0	0.0	0.0	1.4	4	1.3	0.3	3.2	0	0.0	0.0	1.4
	Bronchitis (10006451)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	2	0.6	0.1	2.3	0	0.0	0.0	1.4
	Bronchopneumonia (10006469)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Bullous impetigo (10006563)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Cellulitis (10007882)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	2	0.6	0.1	2.3	1	0.4	0.0	2.1
	Croup infectious (10011416)	0	0.0	0.0	1.2	2	0.8	0.1	2.7	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Cutaneous larva migrans (10059547)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Dengue fever (10012310)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Dysentery (10051402)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	2	0.6	0.1	2.3	0	0.0	0.0	1.4
	Ear infection (10014011)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	5	1.6	0.5	3.7	2	0.7	0.1	2.7
	Gastroenteritis (10017888)	8	2.6	1.1	5.0	4	1.5	0.4	3.8	4	1.3	0.3	3.2	3	1.1	0.2	3.2
	Gingivitis (10018292)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Impetigo (10021531)	1	0.3	0.0	1.8	2	0.8	0.1	2.7	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Infection parasitic (10021857)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Injection site cellulitis (10050057)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Laryngitis (10023874)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Lung infection (10061229)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Nasopharyngitis (10028810)	49	15.7	11.9	20.2	44	16.7	12.4	21.7	53	16.9	12.9	21.5	50	18.6	14.1	23.8
	Otitis media (10033078)	0	0.0	0.0	1.2	3	1.1	0.2	3.3	4	1.3	0.3	3.2	1	0.4	0.0	2.1
	Otitis media acute (10033079)	3	1.0	0.2	2.8	1	0.4	0.0	2.1	3	1.0	0.2	2.8	0	0.0	0.0	1.4
	Parasitic gastroenteritis (10067720)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	1	0.3	0.0	1.8	1	0.4	0.0	2.1
	Pharyngitis (10034835)	5	1.6	0.5	3.7	8	3.0	1.3	5.9	4	1.3	0.3	3.2	3	1.1	0.2	3.2
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Pneumonia (10035664)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Rhinitis (10039083)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	4	1.3	0.3	3.2	0	0.0	0.0	1.4
	Roseola (10039222)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Scarlet fever (10039587)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Sinusitis (10040753)	2	0.6	0.1	2.3	3	1.1	0.2	3.3	3	1.0	0.2	2.8	1	0.4	0.0	2.1
	Subcutaneous abscess (10042343)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Tinea pedis (10043873)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Tonsillitis (10044008)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	3	1.0	0.2	2.8	0	0.0	0.0	1.4
	Tooth abscess (10044016)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Upper respiratory tract infection (10046306)	5	1.6	0.5	3.7	3	1.1	0.2	3.3	6	1.9	0.7	4.1	5	1.9	0.6	4.3
	Viral infection (10047461)	3	1.0	0.2	2.8	2	0.8	0.1	2.7	1	0.3	0.0	1.8	1	0.4	0.0	2.1
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Face injury (10050392)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Joint injury (10060820)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Lethargy (10024264)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	1	0.4	0.0	2.1
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	2	0.7	0.1	2.7
	Bronchial hyperreactivity (10066091)	1	0.3	0.0	1.8	4	1.5	0.4	3.8	2	0.6	0.1	2.3	3	1.1	0.2	3.2
	Cough (10011224)	6	1.9	0.7	4.1	8	3.0	1.3	5.9	3	1.0	0.2	2.8	3	1.1	0.2	3.2
	Nasal congestion (10028735)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Rhinitis allergic (10039085)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Rhinorrhoea (10039101)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	2	0.6	0.1	2.3	2	0.7	0.1	2.7
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	0	0.0	0.0	1.2	2	0.8	0.1	2.7	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Dermatitis (10012431)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Dermatitis contact (10012442)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Dermatitis diaper (10012444)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Dermatosis (10048768)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	2	0.7	0.1	2.7
	Dry skin (10013786)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Ecchymosis (10014080)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Eczema (10014184)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	3	1.0	0.2	2.8	0	0.0	0.0	1.4
	Erythema (10015150)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	2	0.6	0.1	2.3	1	0.4	0.0	2.1

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Onychoclasis (10048886)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Prurigo (10037083)	2	0.6	0.1	2.3	1	0.4	0.0	2.1	3	1.0	0.2	2.8	0	0.0	0.0	1.4
	Rash (10037844)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	1	0.3	0.0	1.8	3	1.1	0.2	3.2
	Rash generalised (10037858)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Swelling face (10042682)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Urticaria (10046735)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	1	0.3	0.0	1.8	1	0.4	0.0	2.1

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "FEVER" which was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.
**Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 137 Global Summary of unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
Number of subjects with at least one unsolicited symptom reported	74	68	93	72	167	140
Number of doses followed by at least one unsolicited symptom	103	90	120	89	223	179
Number of unsolicited symptoms classified by MedDRA Preferred Term*	162	133	188	131	350	264
Number of unsolicited symptoms reported**	171	137	195	132	366	269

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 138 Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		4	2.5	0.7	6.4	5	3.5	1.2	8.0	3	1.9	0.4	5.4	2	1.4	0.2	5.0
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Ear infection (10014011)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Gastroenteritis (10017888)	2	1.3	0.2	4.5	2	1.4	0.2	5.0	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Nasopharyngitis (10028810)	1	0.6	0.0	3.5	2	1.4	0.2	5.0	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Otitis media acute (10033079)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Tonsillitis (10044008)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Skin and subcutaneous tissue disorders (10040785)	Erythema (10015150)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Rash (10037844)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Urticaria (10046735)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 139 Percentage of doses with grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		4	1.3	0.4	3.2	6	2.3	0.8	4.9	3	1.0	0.2	2.8	2	0.7	0.1	2.7
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Ear infection (10014011)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Gastroenteritis (10017888)	2	0.6	0.1	2.3	2	0.8	0.1	2.7	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Nasopharyngitis (10028810)	1	0.3	0.0	1.8	2	0.8	0.1	2.7	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Otitis media acute (10033079)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Tonsillitis (10044008)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Skin and subcutaneous tissue disorders (10040785)	Erythema (10015150)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Rash (10037844)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Urticaria (10046735)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 140 Global Summary of grade 3 unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
Number of subjects with at least one unsolicited symptom reported	4	5	3	2	7	7
Number of doses followed by at least one unsolicited symptom	4	6	3	2	7	8
Number of unsolicited symptoms classified by MedDRA Preferred Term*	4	8	5	2	9	10
Number of unsolicited symptoms reported**	4	9	5	2	9	11

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 141 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		10	6.4	3.1	11.4	7	4.9	2.0	9.9	8	5.0	2.2	9.6	5	3.5	1.2	8.0
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	2	1.3	0.2	4.5	3	2.1	0.4	6.0	4	2.5	0.7	6.3	0	0.0	0.0	2.6
	Faeces hard (10016101)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Vomiting (10047700)	2	1.3	0.2	4.5	0	0.0	0.0	2.6	3	1.9	0.4	5.4	1	0.7	0.0	3.9
General disorders and administration site conditions (10018065)	Injection site rash (10022094)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Pyrexia (10037660)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Ear infection (10014011)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Injection site cellulitis (10050057)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Nasopharyngitis (10028810)	4	2.5	0.7	6.4	1	0.7	0.0	3.9	1	0.6	0.0	3.4	1	0.7	0.0	3.9
	Upper respiratory tract infection (10046306)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Nasal congestion (10028735)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Rhinorrhoea (10039101)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Erythema (10015150)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Rash (10037844)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 142 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		11	3.5	1.8	6.2	7	2.7	1.1	5.4	9	2.9	1.3	5.4	5	1.9	0.6	4.3
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	2	0.6	0.1	2.3	3	1.1	0.2	3.3	4	1.3	0.3	3.2	0	0.0	0.0	1.4
	Faeces hard (10016101)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Vomiting (10047700)	2	0.6	0.1	2.3	0	0.0	0.0	1.4	3	1.0	0.2	2.8	1	0.4	0.0	2.1
General disorders and administration site conditions (10018065)	Injection site rash (10022094)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Pyrexia (10037660)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Ear infection (10014011)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Injection site cellulitis (10050057)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Nasopharyngitis (10028810)	4	1.3	0.4	3.2	1	0.4	0.0	2.1	1	0.3	0.0	1.8	1	0.4	0.0	2.1
	Upper respiratory tract infection (10046306)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	2	0.6	0.1	2.3	0	0.0	0.0	1.4
	Nasal congestion (10028735)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Rhinorrhoea (10039101)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Erythema (10015150)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Rash (10037844)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 143 Global Summary of unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
Number of subjects with at least one unsolicited symptom reported	10	7	8	5	18	12
Number of doses followed by at least one unsolicited symptom	11	7	9	5	20	12
Number of unsolicited symptoms classified by MedDRA Preferred Term*	15	8	16	5	31	13
Number of unsolicited symptoms reported**	17	8	17	5	34	13

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 144 Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Infections and infestations (10021881)	Nasopharyngitis (10028810)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 145 Percentage of doses with grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Infections and infestations (10021881)	Nasopharyngitis (10028810)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 146 Global Summary of grade 3 unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
Number of subjects with at least one unsolicited symptom reported	1	0	0	0	1	0
Number of doses followed by at least one unsolicited symptom	1	0	0	0	1	0
Number of unsolicited symptoms classified by MedDRA Preferred Term*	1	0	0	0	1	0
Number of unsolicited symptoms reported**	1	0	0	0	1	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 147 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		54	34.4	27.0	42.4	43	30.3	22.9	38.5	63	39.4	31.8	47.4	38	26.8	19.7	34.8
---------- ( )	---------- ( )	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1*	0.7	0.0	3.9
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Eye disorders (10015919)	Conjunctivitis (10010741)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	10	6.4	3.1	11.4	8	5.6	2.5	10.8	13	8.1	4.4	13.5	9	6.3	2.9	11.7
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Stomatitis (10042128)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Vomiting (10047700)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	4	2.5	0.7	6.4	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Acute sinusitis (10001076)	3	1.9	0.4	5.5	1	0.7	0.0	3.9	2	1.3	0.2	4.4	1	0.7	0.0	3.9
	Acute tonsillitis (10001093)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Ascariasis (10003442)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Blastocystis infection (10005092)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Bronchiolitis (10006448)	4	2.5	0.7	6.4	0	0.0	0.0	2.6	4	2.5	0.7	6.3	0	0.0	0.0	2.6
	Bronchitis (10006451)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	2	1.3	0.2	4.4	0	0.0	0.0	2.6
	Bronchopneumonia (10006469)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Bullous impetigo (10006563)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Cellulitis (10007882)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	2	1.3	0.2	4.4	1	0.7	0.0	3.9
	Croup infectious (10011416)	0	0.0	0.0	2.3	2	1.4	0.2	5.0	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Cutaneous larva migrans (10059547)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Dengue fever (10012310)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Dysentery (10051402)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	2	1.3	0.2	4.4	0	0.0	0.0	2.6
	Ear infection (10014011)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	5	3.1	1.0	7.1	1	0.7	0.0	3.9
	Gastroenteritis (10017888)	6	3.8	1.4	8.1	2	1.4	0.2	5.0	2	1.3	0.2	4.4	3	2.1	0.4	6.0
	Gingivitis (10018292)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Impetigo (10021531)	0	0.0	0.0	2.3	2	1.4	0.2	5.0	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Injection site cellulitis (10050057)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Laryngitis (10023874)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Lung infection (10061229)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Nasopharyngitis (10028810)	30	19.1	13.3	26.1	22	15.5	10.0	22.5	31	19.4	13.6	26.4	23	16.2	10.6	23.3
	Otitis media (10033078)	0	0.0	0.0	2.3	3	2.1	0.4	6.0	3	1.9	0.4	5.4	1	0.7	0.0	3.9
	Otitis media acute (10033079)	2	1.3	0.2	4.5	1	0.7	0.0	3.9	3	1.9	0.4	5.4	0	0.0	0.0	2.6
	Parasitic gastroenteritis (10067720)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Pharyngitis (10034835)	5	3.2	1.0	7.3	6	4.2	1.6	9.0	4	2.5	0.7	6.3	2	1.4	0.2	5.0
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Rhinitis (10039083)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	4	2.5	0.7	6.3	0	0.0	0.0	2.6
	Scarlet fever (10039587)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Sinusitis (10040753)	2	1.3	0.2	4.5	3	2.1	0.4	6.0	3	1.9	0.4	5.4	1	0.7	0.0	3.9
	Tinea pedis (10043873)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Tonsillitis (10044008)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	3	1.9	0.4	5.4	0	0.0	0.0	2.6
	Tooth abscess (10044016)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Upper respiratory tract infection (10046306)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Viral infection (10047461)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Face injury (10050392)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
	Joint injury (10060820)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	2	1.4	0.2	5.0
	Bronchial hyperreactivity (10066091)	1	0.6	0.0	3.5	4	2.8	0.8	7.1	2	1.3	0.2	4.4	3	2.1	0.4	6.0
	Cough (10011224)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	1	0.6	0.0	3.4	1	0.7	0.0	3.9

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rhinitis allergic (10039085)	0	0.0	0.0	2.3	1	0.7	0.0	3.9	1	0.6	0.0	3.4	0	0.0	0.0	2.6
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Dermatosis (10048768)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	1	0.7	0.0	3.9
	Eczema (10014184)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Onychoclasis (10048886)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Prurigo (10037083)	2	1.3	0.2	4.5	1	0.7	0.0	3.9	2	1.3	0.2	4.4	0	0.0	0.0	2.6
	Rash (10037844)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	1	0.7	0.0	3.9
	Urticaria (10046735)	1	0.6	0.0	3.5	1	0.7	0.0	3.9	1	0.6	0.0	3.4	1	0.7	0.0	3.9

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 148 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		64	20.5	16.2	25.4	55	20.8	16.1	26.2	69	22.0	17.5	27.0	42	15.6	11.5	20.5
---------- ( )	---------- ( )	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1*	0.4	0.0	2.1
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Eye disorders (10015919)	Conjunctivitis (10010741)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	10	3.2	1.5	5.8	8	3.0	1.3	5.9	13	4.1	2.2	7.0	9	3.3	1.5	6.3
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Stomatitis (10042128)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Vomiting (10047700)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	4	1.3	0.4	3.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Acute sinusitis (10001076)	3	1.0	0.2	2.8	1	0.4	0.0	2.1	2	0.6	0.1	2.3	1	0.4	0.0	2.1
	Acute tonsillitis (10001093)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Ascariasis (10003442)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Blastocystis infection (10005092)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Bronchiolitis (10006448)	4	1.3	0.4	3.2	0	0.0	0.0	1.4	4	1.3	0.3	3.2	0	0.0	0.0	1.4
	Bronchitis (10006451)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	2	0.6	0.1	2.3	0	0.0	0.0	1.4
	Bronchopneumonia (10006469)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Bullous impetigo (10006563)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Cellulitis (10007882)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	2	0.6	0.1	2.3	1	0.4	0.0	2.1
	Croup infectious (10011416)	0	0.0	0.0	1.2	2	0.8	0.1	2.7	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Cutaneous larva migrans (10059547)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Dengue fever (10012310)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Dysentery (10051402)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	2	0.6	0.1	2.3	0	0.0	0.0	1.4
	Ear infection (10014011)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	5	1.6	0.5	3.7	2	0.7	0.1	2.7
	Gastroenteritis (10017888)	6	1.9	0.7	4.1	2	0.8	0.1	2.7	2	0.6	0.1	2.3	3	1.1	0.2	3.2
	Gingivitis (10018292)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Impetigo (10021531)	0	0.0	0.0	1.2	2	0.8	0.1	2.7	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Injection site cellulitis (10050057)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Laryngitis (10023874)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Lung infection (10061229)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Nasopharyngitis (10028810)	31	9.9	6.9	13.8	26	9.8	6.5	14.1	31	9.9	6.8	13.7	25	9.3	6.1	13.4
	Otitis media (10033078)	0	0.0	0.0	1.2	3	1.1	0.2	3.3	3	1.0	0.2	2.8	1	0.4	0.0	2.1
	Otitis media acute (10033079)	2	0.6	0.1	2.3	1	0.4	0.0	2.1	3	1.0	0.2	2.8	0	0.0	0.0	1.4
	Parasitic gastroenteritis (10067720)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Pharyngitis (10034835)	5	1.6	0.5	3.7	8	3.0	1.3	5.9	4	1.3	0.3	3.2	2	0.7	0.1	2.7
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Rhinitis (10039083)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	4	1.3	0.3	3.2	0	0.0	0.0	1.4
	Scarlet fever (10039587)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Sinusitis (10040753)	2	0.6	0.1	2.3	3	1.1	0.2	3.3	3	1.0	0.2	2.8	1	0.4	0.0	2.1
	Tinea pedis (10043873)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Tonsillitis (10044008)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	3	1.0	0.2	2.8	0	0.0	0.0	1.4
	Tooth abscess (10044016)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Upper respiratory tract infection (10046306)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Viral infection (10047461)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Face injury (10050392)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
	Joint injury (10060820)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	2	0.7	0.1	2.7
	Bronchial hyperreactivity (10066091)	1	0.3	0.0	1.8	4	1.5	0.4	3.8	2	0.6	0.1	2.3	3	1.1	0.2	3.2
	Cough (10011224)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	1	0.3	0.0	1.8	1	0.4	0.0	2.1

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rhinitis allergic (10039085)	0	0.0	0.0	1.2	1	0.4	0.0	2.1	1	0.3	0.0	1.8	0	0.0	0.0	1.4
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Dermatosis (10048768)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	1	0.4	0.0	2.1
	Eczema (10014184)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Onychoclasis (10048886)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Prurigo (10037083)	2	0.6	0.1	2.3	1	0.4	0.0	2.1	3	1.0	0.2	2.8	0	0.0	0.0	1.4
	Rash (10037844)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	1	0.4	0.0	2.1
	Urticaria (10046735)	1	0.3	0.0	1.8	1	0.4	0.0	2.1	1	0.3	0.0	1.8	1	0.4	0.0	2.1

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 149 Global Summary of unsolicited adverse events reported with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	6-17M	**18-35M**	**6-17M**	**18-35M**	**6-17M**	**18-35M**
Number of subjects with at least one unsolicited symptom reported	54	43	63	38	117	81
Number of doses followed by at least one unsolicited symptom	64	55	69	42	133	97
Number of unsolicited symptoms classified by MedDRA Preferred Term*	86	77	105	63	191	140
Number of unsolicited symptoms reported**	87	79	105	63	192	142

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 150 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 157				18-35M N = 142				6-17M N = 160				18-35M N = 142			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		1	0.6	0.0	3.5	0	0.0	0.0	2.6	2	1.3	0.2	4.4	0	0.0	0.0	2.6
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.6	0.0	3.5	0	0.0	0.0	2.6	0	0.0	0.0	2.3	0	0.0	0.0	2.6
Infections and infestations (10021881)	Blastocystis infection (10005092)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	1	0.6	0.0	3.4	0	0.0	0.0	2.6
	Bronchiolitis (10006448)	0	0.0	0.0	2.3	0	0.0	0.0	2.6	2	1.3	0.2	4.4	0	0.0	0.0	2.6

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine; 6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 151 Percentage of doses with serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		6-17M N = 312				18-35M N = 264				6-17M N = 314				18-35M N = 269			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		1	0.3	0.0	1.8	0	0.0	0.0	1.4	2	0.6	0.1	2.3	0	0.0	0.0	1.4
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.3	0.0	1.8	0	0.0	0.0	1.4	0	0.0	0.0	1.2	0	0.0	0.0	1.4
Infections and infestations (10021881)	Blastocystis infection (10005092)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	1	0.3	0.0	1.8	0	0.0	0.0	1.4
	Bronchiolitis (10006448)	0	0.0	0.0	1.2	0	0.0	0.0	1.4	2	0.6	0.1	2.3	0	0.0	0.0	1.4

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine; 6-17M = 6-17 months old subjects; 18-35M = 18-35 months old subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 152 Global Summary of serious adverse events reported within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
Number of subjects with at least one unsolicited symptom reported	1	0	2	0	3	0
Number of doses followed by at least one unsolicited symptom	1	0	2	0	3	0
Number of unsolicited symptoms classified by MedDRA Preferred Term*	1	0	3	0	4	0
Number of unsolicited symptoms reported**	1	0	3	0	4	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 153 Percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

No records exist in this table

Table 154 Listing of potential Immune-Mediated Disease reported within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

No records exist in this table

Table 155 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom during the 7-day post-vaccination period (By age strata 6-17M- Total Vaccinated cohort)

								Relative Risk (Q-QIV/6-17M over D-TIV-YB/6-17M)			
		Q-QIV/6-17M			D-TIV-YB/6-17M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Drowsiness	All	154	40	26.0	155	39	25.2	1.03	0.71	1.51	0.8968
	Grade 3	154	2	1.3	155	3	1.9	0.67	0.14	3.32	1.0000
Irritability / fussiness	All	154	49	31.8	155	50	32.3	0.99	0.71	1.36	1.0000
	Grade 3	154	6	3.9	155	9	5.8	0.67	0.25	1.77	0.5981
Loss of appetite	All	154	38	24.7	155	33	21.3	1.16	0.77	1.74	0.5014
	Grade 3	154	2	1.3	155	4	2.6	0.50	0.11	2.32	0.6844
Dose 2											
Drowsiness	All	151	24	15.9	149	19	12.8	1.25	0.72	2.17	0.5107
	Grade 3	151	2	1.3	149	4	2.7	0.49	0.11	2.27	0.4460
Irritability / fussiness	All	151	37	24.5	149	39	26.2	0.94	0.64	1.38	0.7912
	Grade 3	151	3	2.0	149	4	2.7	0.74	0.19	2.92	0.7219
Loss of appetite	All	151	30	19.9	149	26	17.4	1.14	0.71	1.83	0.6574
	Grade 3	151	6	4.0	149	3	2.0	1.97	0.55	7.12	0.5012
Overall/dose											
Drowsiness	All	305	64	21.0	304	58	19.1	1.10	0.80	1.51	0.6129
	Grade 3	305	4	1.3	304	7	2.3	0.57	0.18	1.80	0.3829
Irritability / fussiness	All	305	86	28.2	304	89	29.3	0.96	0.75	1.24	0.7887
	Grade 3	305	9	3.0	304	13	4.3	0.69	0.31	1.55	0.3957
Loss of appetite	All	305	68	22.3	304	59	19.4	1.15	0.84	1.57	0.4251
	Grade 3	305	8	2.6	304	7	2.3	1.14	0.43	2.99	1.0000
Overall/subject											
Drowsiness	All	155	51	32.9	155	48	31.0	1.06	0.77	1.47	0.8076
	Grade 3	155	4	2.6	155	7	4.5	0.57	0.18	1.79	0.5414
Irritability / fussiness	All	155	63	40.6	155	66	42.6	0.95	0.73	1.24	0.8178
	Grade 3	155	8	5.2	155	12	7.7	0.67	0.29	1.55	0.4889
Loss of appetite	All	155	52	33.5	155	46	29.7	1.13	0.81	1.57	0.5415
	Grade 3	155	8	5.2	155	7	4.5	1.14	0.44	2.97	1.0000

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
6-17M = 6-17 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 156 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom during the 7-day post-vaccination period (By age strata 18-35M- Total Vaccinated cohort)

								Relative Risk (Q-QIV/18-35M over D-TIV-YB/18-35M)			
		Q-QIV/18-35M			D-TIV-YB/18-35M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Drowsiness	All	135	32	23.7	141	25	17.7	1.34	0.84	2.13	0.2369
	Grade 3	135	4	3.0	141	1	0.7	4.18	0.64	27.70	0.2055
Irritability / fussiness	All	135	42	31.1	141	44	31.2	1.00	0.70	1.41	1.0000
	Grade 3	135	5	3.7	141	1	0.7	5.22	0.82	33.60	0.1139
Loss of appetite	All	135	40	29.6	141	38	27.0	1.10	0.76	1.60	0.6887
	Grade 3	135	7	5.2	141	3	2.1	2.44	0.70	8.54	0.2094
Dose 2											
Drowsiness	All	121	25	20.7	127	25	19.7	1.05	0.64	1.72	0.8753
	Grade 3	121	1	0.8	127	1	0.8	1.05	0.11	10.02	1.0000
Irritability / fussiness	All	121	35	28.9	127	36	28.3	1.02	0.69	1.51	1.0000
	Grade 3	121	3	2.5	127	1	0.8	3.15	0.46	21.89	0.3602
Loss of appetite	All	121	18	14.9	127	29	22.8	0.65	0.38	1.10	0.1442
	Grade 3	121	2	1.7	127	5	3.9	0.42	0.09	1.84	0.4474
Overall/dose											
Drowsiness	All	256	57	22.3	268	50	18.7	1.19	0.85	1.67	0.3301
	Grade 3	256	5	2.0	268	2	0.7	2.62	0.59	11.64	0.2756
Irritability / fussiness	All	256	77	30.1	268	80	29.9	1.01	0.78	1.31	1.0000
	Grade 3	256	8	3.1	268	2	0.7	4.19	1.02	17.35	0.0578
Loss of appetite	All	256	58	22.7	268	67	25.0	0.91	0.67	1.23	0.5402
	Grade 3	256	9	3.5	268	8	3.0	1.18	0.48	2.92	0.8080
Overall/subject											
Drowsiness	All	135	42	31.1	141	40	28.4	1.10	0.76	1.58	0.6929
	Grade 3	135	5	3.7	141	2	1.4	2.61	0.59	11.56	0.2735
Irritability / fussiness	All	135	55	40.7	141	57	40.4	1.01	0.76	1.34	1.0000
	Grade 3	135	7	5.2	141	2	1.4	3.66	0.88	15.35	0.0973
Loss of appetite	All	135	47	34.8	141	54	38.3	0.91	0.66	1.24	0.6173
	Grade 3	135	8	5.9	141	7	5.0	1.19	0.46	3.10	0.7945

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 157 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited local symptom during the 7-day post-vaccination period (By age strata - Total Vaccinated cohort)

								Relative Risk (Q-QIV/6-17M over D-TIV-YB/6-17M)			
		Q-QIV/6-17M			D-TIV-YB/6-17M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Pain	All	154	25	16.2	156	19	12.2	1.33	0.77	2.31	0.3321
	Grade 3	154	2	1.3	156	1	0.6	2.03	0.27	15.42	0.6214
Redness (mm)	All	154	2	1.3	156	1	0.6	2.03	0.27	15.42	0.6214
	>100	154	0	0.0	156	0	0.0	INF	0.00	INF	
Swelling (mm)	All	154	2	1.3	156	1	0.6	2.03	0.27	15.42	0.6214
	>100	154	0	0.0	156	0	0.0	INF	0.00	INF	
Dose 2											
Pain	All	153	25	16.3	149	19	12.8	1.28	0.74	2.22	0.4171
	Grade 3	153	2	1.3	149	1	0.7	1.95	0.26	14.82	1.0000
Redness (mm)	All	153	3	2.0	149	2	1.3	1.46	0.30	7.25	1.0000
	>100	153	0	0.0	149	0	0.0	INF	0.00	INF	
Swelling (mm)	All	153	4	2.6	149	2	1.3	1.95	0.42	9.02	0.6845
	>100	153	0	0.0	149	0	0.0	INF	0.00	INF	
Overall/dose											
Pain	All	307	50	16.3	305	38	12.5	1.31	0.89	1.93	0.2051
	Grade 3	307	4	1.3	305	2	0.7	1.99	0.43	9.24	0.6860
Redness (mm)	All	307	5	1.6	305	3	1.0	1.66	0.44	6.23	0.7248
	>100	307	0	0.0	305	0	0.0	INF	0.00	INF	
Swelling (mm)	All	307	6	2.0	305	3	1.0	1.99	0.55	7.21	0.5046
	>100	307	0	0.0	305	0	0.0	INF	0.00	INF	
Overall/subject											
Pain	All	155	39	25.2	156	31	19.9	1.27	0.84	1.92	0.2800
	Grade 3	155	4	2.6	156	1	0.6	4.03	0.61	26.70	0.2142
Redness (mm)	All	155	4	2.6	156	3	1.9	1.34	0.34	5.30	0.7230
	>100	155	0	0.0	156	0	0.0	INF	0.00	INF	
Swelling (mm)	All	155	5	3.2	156	2	1.3	2.52	0.57	11.15	0.2827
	>100	155	0	0.0	156	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 158 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited local symptom during the 7-day post-vaccination period (By age strata - Total Vaccinated cohort)

								Relative Risk (Q-QIV/18-35M over D-TIV-YB/18-35M)			
		Q-QIV/18-35M			D-TIV-YB/18-35M				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Dose 1											
Pain	All	136	48	35.3	141	45	31.9	1.11	0.79	1.54	0.6112
	Grade 3	136	3	2.2	141	0	0.0	INF	0.82	INF	0.1170
Redness (mm)	All	136	1	0.7	141	1	0.7	1.04	0.11	9.90	1.0000
	>100	136	0	0.0	141	0	0.0	INF	0.00	INF	
Swelling (mm)	All	136	0	0.0	141	1	0.7	0.00	0.00	3.97	1.0000
	>100	136	0	0.0	141	0	0.0	INF	0.00	INF	
Dose 2											
Pain	All	121	32	26.4	127	40	31.5	0.84	0.57	1.24	0.4038
	Grade 3	121	1	0.8	127	2	1.6	0.52	0.07	3.97	1.0000
Redness (mm)	All	121	1	0.8	127	2	1.6	0.52	0.07	3.97	1.0000
	>100	121	0	0.0	127	0	0.0	INF	0.00	INF	
Swelling (mm)	All	121	0	0.0	127	3	2.4	0.00	0.00	1.33	0.2474
	>100	121	0	0.0	127	0	0.0	INF	0.00	INF	
Overall/dose											
Pain	All	257	80	31.1	268	85	31.7	0.98	0.76	1.26	0.9252
	Grade 3	257	4	1.6	268	2	0.7	2.09	0.45	9.69	0.4415
Redness (mm)	All	257	2	0.8	268	3	1.1	0.70	0.14	3.46	1.0000
	>100	257	0	0.0	268	0	0.0	INF	0.00	INF	
Swelling (mm)	All	257	0	0.0	268	4	1.5	0.00	0.00	1.00	0.1239
	>100	257	0	0.0	268	0	0.0	INF	0.00	INF	
Overall/subject											
Pain	All	136	56	41.2	141	60	42.6	0.97	0.73	1.28	0.9031
	Grade 3	136	3	2.2	141	2	1.4	1.56	0.31	7.72	0.6797
Redness (mm)	All	136	2	1.5	141	3	2.1	0.69	0.14	3.42	1.0000
	>100	136	0	0.0	141	0	0.0	INF	0.00	INF	
Swelling (mm)	All	136	0	0.0	141	4	2.8	0.00	0.00	0.98	0.1225
	>100	136	0	0.0	141	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 159 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 48 hours of the vaccinations (By age strata 6-17M - Total Vaccinated cohort)

								Relative Risk (Q-QIV/6-17M over D-TIV-YB/6-17M)			
		Q-QIV/6-17M			D-TIV-YB/6-17M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	154	9	5.8	155	11	7.1	0.82	0.36	1.89	0.8178
	≥38	154	8	5.2	155	11	7.1	0.73	0.31	1.72	0.6369
	≥38.5	154	2	1.3	155	2	1.3	1.01	0.18	5.66	1.0000
	≥39.0	154	2	1.3	155	0	0.0	INF	0.53	INF	0.2476
	≥40.0	154	0	0.0	155	0	0.0	INF	0.00	INF	
	Related	154	8	5.2	155	11	7.1	0.73	0.31	1.72	0.6369
	≥38 Related	154	7	4.5	155	11	7.1	0.64	0.26	1.56	0.4673
	≥38.5 Related	154	1	0.6	155	2	1.3	0.50	0.07	3.82	1.0000
	≥39.0 Related	154	1	0.6	155	0	0.0	INF	0.26	INF	0.4984
	≥40.0 Related	154	0	0.0	155	0	0.0	INF	0.00	INF	
Dose 2											
Temperature/(Axillary) (°C)	All	151	11	7.3	149	8	5.4	1.36	0.58	3.20	0.6367
	≥38	151	11	7.3	149	8	5.4	1.36	0.58	3.20	0.6367
	≥38.5	151	6	4.0	149	2	1.3	2.96	0.69	12.72	0.2825
	≥39.0	151	5	3.3	149	1	0.7	4.93	0.77	31.75	0.2141
	≥40.0	151	0	0.0	149	0	0.0	INF	0.00	INF	
	Related	151	10	6.6	149	7	4.7	1.41	0.57	3.51	0.6189
	≥38 Related	151	10	6.6	149	7	4.7	1.41	0.57	3.51	0.6189
	≥38.5 Related	151	5	3.3	149	1	0.7	4.93	0.77	31.75	0.2141
	≥39.0 Related	151	4	2.6	149	0	0.0	INF	1.04	INF	0.1225
	≥40.0 Related	151	0	0.0	149	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	305	20	6.6	304	19	6.3	1.05	0.58	1.91	1.0000
	≥38	305	19	6.2	304	19	6.3	1.00	0.54	1.83	1.0000
	≥38.5	305	8	2.6	304	4	1.3	1.99	0.65	6.18	0.3829
	≥39.0	305	7	2.3	304	1	0.3	6.98	1.13	43.40	0.0685
	≥40.0	305	0	0.0	304	0	0.0	INF	0.00	INF	
	Related	305	18	5.9	304	18	5.9	1.00	0.53	1.86	1.0000
	≥38 Related	305	17	5.6	304	18	5.9	0.94	0.50	1.77	0.8639
	≥38.5 Related	305	6	2.0	304	3	1.0	1.99	0.55	7.23	0.5046
	≥39.0 Related	305	5	1.6	304	0	0.0	INF	1.30	INF	0.0615
	≥40.0 Related	305	0	0.0	304	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	155	16	10.3	155	18	11.6	0.89	0.47	1.66	0.8561
	≥38	155	15	9.7	155	18	11.6	0.83	0.44	1.58	0.7131
	≥38.5	155	8	5.2	155	4	2.6	2.00	0.65	6.16	0.3781
	≥39.0	155	7	4.5	155	1	0.6	7.00	1.14	43.48	0.0668
	≥40.0	155	0	0.0	155	0	0.0	INF	0.00	INF	
	Related	155	14	9.0	155	17	11.0	0.82	0.42	1.59	0.7055
	≥38 Related	155	13	8.4	155	17	11.0	0.76	0.39	1.50	0.5650
	≥38.5 Related	155	6	3.9	155	3	1.9	2.00	0.56	7.22	0.5013
	≥39.0 Related	155	5	3.2	155	0	0.0	INF	1.32	INF	0.0605
	≥40.0 Related	155	0	0.0	155	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
6-17M = 6-17 months old subjects

For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 160 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 48 hours of the vaccinations (By age strata 18-35M - Total Vaccinated cohort)

								Relative Risk (Q-QIV/18-35M over D-TIV-YB/18-35M)			
		Q-QIV/18-35M			D-TIV-YB/18-35M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	135	13	9.6	141	7	5.0	1.94	0.82	4.61	0.1657
	≥38	135	11	8.1	141	6	4.3	1.91	0.76	4.89	0.2150
	≥38.5	135	7	5.2	141	4	2.8	1.83	0.58	5.75	0.3690
	≥39.0	135	2	1.5	141	2	1.4	1.04	0.19	5.87	1.0000
	≥40.0	135	0	0.0	141	0	0.0	INF	0.00	INF	
	Related	135	13	9.6	141	6	4.3	2.26	0.92	5.63	0.0970
	≥38 Related	135	11	8.1	141	5	3.5	2.30	0.86	6.21	0.1251
	≥38.5 Related	135	7	5.2	141	3	2.1	2.44	0.70	8.54	0.2094
	≥39.0 Related	135	2	1.5	141	2	1.4	1.04	0.19	5.87	1.0000
	≥40.0 Related	135	0	0.0	141	0	0.0	INF	0.00	INF	
Dose 2											
Temperature/(Axillary) (°C)	All	121	5	4.1	127	4	3.1	1.31	0.39	4.44	0.7442
	≥38	121	5	4.1	127	4	3.1	1.31	0.39	4.44	0.7442
	≥38.5	121	4	3.3	127	0	0.0	INF	1.11	INF	0.0552
	≥39.0	121	0	0.0	127	0	0.0	INF	0.00	INF	
	≥40.0	121	0	0.0	127	0	0.0	INF	0.00	INF	
	Related	121	5	4.1	127	4	3.1	1.31	0.39	4.44	0.7442
	≥38 Related	121	5	4.1	127	4	3.1	1.31	0.39	4.44	0.7442
	≥38.5 Related	121	4	3.3	127	0	0.0	INF	1.11	INF	0.0552
	≥39.0 Related	121	0	0.0	127	0	0.0	INF	0.00	INF	
	≥40.0 Related	121	0	0.0	127	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	256	18	7.0	268	11	4.1	1.71	0.84	3.51	0.1810
	≥38	256	16	6.3	268	10	3.7	1.68	0.79	3.57	0.2282
	≥38.5	256	11	4.3	268	4	1.5	2.88	0.98	8.49	0.0673
	≥39.0	256	2	0.8	268	2	0.7	1.05	0.19	5.91	1.0000
	≥40.0	256	0	0.0	268	0	0.0	INF	0.00	INF	
	Related	256	18	7.0	268	10	3.7	1.88	0.90	3.95	0.1196
	≥38 Related	256	16	6.3	268	9	3.4	1.86	0.86	4.06	0.1515
	≥38.5 Related	256	11	4.3	268	3	1.1	3.84	1.17	12.70	0.0296
	≥39.0 Related	256	2	0.8	268	2	0.7	1.05	0.19	5.91	1.0000
	≥40.0 Related	256	0	0.0	268	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	135	17	12.6	141	11	7.8	1.61	0.80	3.28	0.2324
	≥38	135	15	11.1	141	10	7.1	1.57	0.74	3.32	0.2963
	≥38.5	135	10	7.4	141	4	2.8	2.61	0.89	7.75	0.1029
	≥39.0	135	2	1.5	141	2	1.4	1.04	0.19	5.87	1.0000
	≥40.0	135	0	0.0	141	0	0.0	INF	0.00	INF	
	Related	135	17	12.6	141	10	7.1	1.78	0.86	3.70	0.1564
	≥38 Related	135	15	11.1	141	9	6.4	1.74	0.81	3.79	0.2013
	≥38.5 Related	135	10	7.4	141	3	2.1	3.48	1.06	11.58	0.0476
	≥39.0 Related	135	2	1.5	141	2	1.4	1.04	0.19	5.87	1.0000
	≥40.0 Related	135	0	0.0	141	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine

18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 161 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 4 days post-vaccinations (By age strata 6-17M - Total Vaccinated cohort)

								Relative Risk (Q-QIV/6-17M over D-TIV-YB/6-17M)			
		Q-QIV/6-17M			D-TIV-YB/6-17M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	154	15	9.7	155	19	12.3	0.79	0.42	1.49	0.5861
	≥38	154	15	9.7	155	17	11.0	0.89	0.46	1.70	0.8522
	≥38.5	154	6	3.9	155	5	3.2	1.21	0.40	3.67	0.7699
	≥39.0	154	3	1.9	155	2	1.3	1.51	0.30	7.50	0.6844
	≥40.0	154	0	0.0	155	1	0.6	0.00	0.00	3.86	1.0000
	Related	154	11	7.1	155	16	10.3	0.69	0.34	1.42	0.4209
	≥38 Related	154	11	7.1	155	15	9.7	0.74	0.35	1.53	0.5395
	≥38.5 Related	154	4	2.6	155	4	2.6	1.01	0.28	3.62	1.0000
	≥39.0 Related	154	1	0.6	155	1	0.6	1.01	0.11	9.62	1.0000
	≥40.0 Related	154	0	0.0	155	1	0.6	0.00	0.00	3.86	1.0000
Dose 2											
Temperature/(Axillary) (°C)	All	151	13	8.6	149	13	8.7	0.99	0.48	2.03	1.0000
	≥38	151	12	7.9	149	13	8.7	0.91	0.44	1.90	0.8374
	≥38.5	151	9	6.0	149	9	6.0	0.99	0.41	2.36	1.0000
	≥39.0	151	7	4.6	149	4	2.7	1.73	0.55	5.44	0.5412
	≥40.0	151	0	0.0	149	1	0.7	0.00	0.00	3.78	0.4967
	Related	151	11	7.3	149	11	7.4	0.99	0.45	2.17	1.0000
	≥38 Related	151	11	7.3	149	11	7.4	0.99	0.45	2.17	1.0000
	≥38.5 Related	151	8	5.3	149	7	4.7	1.13	0.43	2.93	1.0000
	≥39.0 Related	151	6	4.0	149	3	2.0	1.97	0.55	7.12	0.5012
	≥40.0 Related	151	0	0.0	149	1	0.7	0.00	0.00	3.78	0.4967
Overall/dose											
Temperature/(Axillary) (°C)	All	305	28	9.2	304	32	10.5	0.87	0.54	1.41	0.5896
	≥38	305	27	8.9	304	30	9.9	0.90	0.55	1.46	0.6791
	≥38.5	305	15	4.9	304	14	4.6	1.07	0.53	2.15	1.0000
	≥39.0	305	10	3.3	304	6	2.0	1.66	0.64	4.36	0.4484
	≥40.0	305	0	0.0	304	2	0.7	0.00	0.00	1.91	0.2488
	Related	305	22	7.2	304	27	8.9	0.81	0.48	1.38	0.4608
	≥38 Related	305	22	7.2	304	26	8.6	0.84	0.49	1.45	0.5517
	≥38.5 Related	305	12	3.9	304	11	3.6	1.09	0.50	2.38	1.0000
	≥39.0 Related	305	7	2.3	304	4	1.3	1.74	0.55	5.54	0.5451
	≥40.0 Related	305	0	0.0	304	2	0.7	0.00	0.00	1.91	0.2488
Overall/subject											
Temperature/(Axillary) (°C)	All	155	23	14.8	155	31	20.0	0.74	0.45	1.21	0.2945
	≥38	155	22	14.2	155	29	18.7	0.76	0.46	1.25	0.3581
	≥38.5	155	14	9.0	155	14	9.0	1.00	0.50	2.00	1.0000
	≥39.0	155	10	6.5	155	6	3.9	1.67	0.64	4.33	0.4423
	≥40.0	155	0	0.0	155	2	1.3	0.00	0.00	1.91	0.4984
	Related	155	18	11.6	155	26	16.8	0.69	0.40	1.20	0.2544
	≥38 Related	155	18	11.6	155	25	16.1	0.72	0.41	1.25	0.3242
	≥38.5 Related	155	11	7.1	155	11	7.1	1.00	0.46	2.20	1.0000
	≥39.0 Related	155	7	4.5	155	4	2.6	1.75	0.56	5.52	0.5414
	≥40.0 Related	155	0	0.0	155	2	1.3	0.00	0.00	1.91	0.4984

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine

6-17M = 6-17 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 162 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 4 days post-vaccinations (By age strata 18-35M - Total Vaccinated cohort)

								Relative Risk (Q-QIV/18-35M over D-TIV-YB/18-35M)			
		Q-QIV/18-35M			D-TIV-YB/18-35M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	135	18	13.3	141	10	7.1	1.88	0.92	3.88	0.1104
	≥38	135	17	12.6	141	9	6.4	1.97	0.93	4.22	0.0990
	≥38.5	135	9	6.7	141	6	4.3	1.57	0.60	4.14	0.4335
	≥39.0	135	3	2.2	141	2	1.4	1.57	0.32	7.77	0.6786
	≥40.0	135	0	0.0	141	0	0.0	INF	0.00	INF	
	Related	135	17	12.6	141	8	5.7	2.22	1.01	4.90	0.0584
	≥38 Related	135	16	11.9	141	7	5.0	2.39	1.04	5.52	0.0493
	≥38.5 Related	135	9	6.7	141	4	2.8	2.35	0.79	7.08	0.1615
	≥39.0 Related	135	3	2.2	141	2	1.4	1.57	0.32	7.77	0.6786
	≥40.0 Related	135	0	0.0	141	0	0.0	INF	0.00	INF	
Dose 2											
Temperature/(Axillary) (°C)	All	121	9	7.4	127	5	3.9	1.89	0.68	5.26	0.2782
	≥38	121	9	7.4	127	5	3.9	1.89	0.68	5.26	0.2782
	≥38.5	121	7	5.8	127	1	0.8	7.35	1.20	45.60	0.0324
	≥39.0	121	3	2.5	127	0	0.0	INF	0.83	INF	0.1147
	≥40.0	121	1	0.8	127	0	0.0	INF	0.27	INF	0.4879
	Related	121	6	5.0	127	4	3.1	1.57	0.49	5.10	0.5319
	≥38 Related	121	6	5.0	127	4	3.1	1.57	0.49	5.10	0.5319
	≥38.5 Related	121	5	4.1	127	0	0.0	INF	1.38	INF	0.0265
	≥39.0 Related	121	2	1.7	127	0	0.0	INF	0.55	INF	0.2370
	≥40.0 Related	121	0	0.0	127	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	256	27	10.5	268	15	5.6	1.88	1.04	3.44	0.0524
	≥38	256	26	10.2	268	14	5.2	1.94	1.05	3.61	0.0472
	≥38.5	256	16	6.3	268	7	2.6	2.39	1.03	5.59	0.0540
	≥39.0	256	6	2.3	268	2	0.7	3.14	0.73	13.54	0.1675
	≥40.0	256	1	0.4	268	0	0.0	INF	0.27	INF	0.4885
	Related	256	23	9.0	268	12	4.5	2.01	1.03	3.91	0.0530
	≥38 Related	256	22	8.6	268	11	4.1	2.09	1.05	4.18	0.0466
	≥38.5 Related	256	14	5.5	268	4	1.5	3.66	1.29	10.50	0.0153
	≥39.0 Related	256	5	2.0	268	2	0.7	2.62	0.59	11.64	0.2756
	≥40.0 Related	256	0	0.0	268	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	135	25	18.5	141	14	9.9	1.87	1.03	3.42	0.0563
	≥38	135	24	17.8	141	13	9.2	1.93	1.04	3.61	0.0510
	≥38.5	135	14	10.4	141	6	4.3	2.44	1.00	6.01	0.0632
	≥39.0	135	6	4.4	141	2	1.4	3.13	0.74	13.46	0.1652
	≥40.0	135	1	0.7	141	0	0.0	INF	0.27	INF	0.4891
	Related	135	21	15.6	141	12	8.5	1.83	0.95	3.54	0.0942
	≥38 Related	135	20	14.8	141	11	7.8	1.90	0.96	3.78	0.0855
	≥38.5 Related	135	12	8.9	141	4	2.8	3.13	1.09	9.07	0.0392
	≥39.0 Related	135	5	3.7	141	2	1.4	2.61	0.59	11.56	0.2735
	≥40.0 Related	135	0	0.0	141	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
18-35M = 18-35 months old subjects

For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 163 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 7 days post-vaccinations (By age strata 6-17M - Total Vaccinated cohort)

								Relative Risk (Q-QIV/6-17M over D-TIV-YB/6-17M)			
		Q-QIV/6-17M			D-TIV-YB/6-17M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	154	20	13.0	155	28	18.1	0.72	0.42	1.21	0.2717
	≥38	154	19	12.3	155	27	17.4	0.71	0.41	1.21	0.2633
	≥38.5	154	8	5.2	155	11	7.1	0.73	0.31	1.72	0.6369
	≥39.0	154	3	1.9	155	6	3.9	0.50	0.14	1.81	0.5013
	≥40.0	154	1	0.6	155	2	1.3	0.50	0.07	3.82	1.0000
	Related	154	14	9.1	155	21	13.5	0.67	0.36	1.26	0.2815
	≥38 Related	154	13	8.4	155	20	12.9	0.65	0.34	1.25	0.2690
	≥38.5 Related	154	5	3.2	155	6	3.9	0.84	0.28	2.54	1.0000
	≥39.0 Related	154	1	0.6	155	2	1.3	0.50	0.07	3.82	1.0000
	≥40.0 Related	154	1	0.6	155	1	0.6	1.01	0.11	9.62	1.0000
Dose 2											
Temperature/(Axillary) (°C)	All	151	19	12.6	149	15	10.1	1.25	0.67	2.35	0.5857
	≥38	151	18	11.9	149	15	10.1	1.18	0.63	2.24	0.7128
	≥38.5	151	14	9.3	149	11	7.4	1.26	0.60	2.64	0.6771
	≥39.0	151	8	5.3	149	5	3.4	1.58	0.56	4.51	0.5725
	≥40.0	151	0	0.0	149	1	0.7	0.00	0.00	3.78	0.4967
	Related	151	15	9.9	149	13	8.7	1.14	0.57	2.28	0.8432
	≥38 Related	151	15	9.9	149	13	8.7	1.14	0.57	2.28	0.8432
	≥38.5 Related	151	12	7.9	149	9	6.0	1.32	0.58	2.97	0.6520
	≥39.0 Related	151	6	4.0	149	4	2.7	1.48	0.46	4.81	0.7498
	≥40.0 Related	151	0	0.0	149	1	0.7	0.00	0.00	3.78	0.4967
Overall/dose											
Temperature/(Axillary) (°C)	All	305	39	12.8	304	43	14.1	0.90	0.61	1.35	0.6369
	≥38	305	37	12.1	304	42	13.8	0.88	0.58	1.32	0.5489
	≥38.5	305	22	7.2	304	22	7.2	1.00	0.57	1.75	1.0000
	≥39.0	305	11	3.6	304	11	3.6	1.00	0.45	2.22	1.0000
	≥40.0	305	1	0.3	304	3	1.0	0.33	0.05	2.31	0.3729
	Related	305	29	9.5	304	34	11.2	0.85	0.53	1.35	0.5091
	≥38 Related	305	28	9.2	304	33	10.9	0.85	0.53	1.36	0.5032
	≥38.5 Related	305	17	5.6	304	15	4.9	1.13	0.58	2.20	0.8562
	≥39.0 Related	305	7	2.3	304	6	2.0	1.16	0.41	3.27	1.0000
	≥40.0 Related	305	1	0.3	304	2	0.7	0.50	0.07	3.79	0.6238
Overall/subject											
Temperature/(Axillary) (°C)	All	155	32	20.6	155	38	24.5	0.84	0.56	1.27	0.4972
	≥38	155	30	19.4	155	37	23.9	0.81	0.53	1.24	0.4078
	≥38.5	155	21	13.5	155	21	13.5	1.00	0.57	1.74	1.0000
	≥39.0	155	11	7.1	155	10	6.5	1.10	0.49	2.47	1.0000
	≥40.0	155	1	0.6	155	3	1.9	0.33	0.05	2.30	0.6226
	Related	155	23	14.8	155	30	19.4	0.77	0.47	1.25	0.3655
	≥38 Related	155	22	14.2	155	29	18.7	0.76	0.46	1.25	0.3581
	≥38.5 Related	155	16	10.3	155	15	9.7	1.07	0.55	2.06	1.0000
	≥39.0 Related	155	7	4.5	155	6	3.9	1.17	0.42	3.25	1.0000
	≥40.0 Related	155	1	0.6	155	2	1.3	0.50	0.07	3.79	1.0000

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine

6-17M = 6-17 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 164 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 7 days post-vaccinations (By age strata 18-35M - Total Vaccinated cohort)

								Relative Risk (Q-QIV/18-35M over D-TIV-YB/18-35M)			
		Q-QIV/18-35M			D-TIV-YB/18-35M				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	135	24	17.8	141	16	11.3	1.57	0.88	2.81	0.1708
	≥38	135	23	17.0	141	16	11.3	1.50	0.84	2.70	0.2261
	≥38.5	135	13	9.6	141	11	7.8	1.23	0.58	2.62	0.6714
	≥39.0	135	8	5.9	141	3	2.1	2.79	0.82	9.56	0.1308
	≥40.0	135	0	0.0	141	0	0.0	INF	0.00	INF	
	Related	135	19	14.1	141	10	7.1	1.98	0.98	4.07	0.0766
	≥38 Related	135	18	13.3	141	10	7.1	1.88	0.92	3.88	0.1104
	≥38.5 Related	135	12	8.9	141	7	5.0	1.79	0.75	4.31	0.2382
	≥39.0 Related	135	7	5.2	141	3	2.1	2.44	0.70	8.54	0.2094
	≥40.0 Related	135	0	0.0	141	0	0.0	INF	0.00	INF	
Dose 2											
Temperature/(Axillary) (°C)	All	121	12	9.9	127	10	7.9	1.26	0.58	2.76	0.6575
	≥38	121	10	8.3	127	10	7.9	1.05	0.46	2.38	1.0000
	≥38.5	121	8	6.6	127	2	1.6	4.20	1.03	17.31	0.0551
	≥39.0	121	4	3.3	127	0	0.0	INF	1.11	INF	0.0552
	≥40.0	121	2	1.7	127	0	0.0	INF	0.55	INF	0.2370
	Related	121	9	7.4	127	8	6.3	1.18	0.48	2.88	0.8043
	≥38 Related	121	7	5.8	127	8	6.3	0.92	0.35	2.37	1.0000
	≥38.5 Related	121	6	5.0	127	1	0.8	6.30	1.01	39.67	0.0609
	≥39.0 Related	121	3	2.5	127	0	0.0	INF	0.83	INF	0.1147
	≥40.0 Related	121	1	0.8	127	0	0.0	INF	0.27	INF	0.4879
Overall/dose											
Temperature/(Axillary) (°C)	All	256	36	14.1	268	26	9.7	1.45	0.91	2.32	0.1374
	≥38	256	33	12.9	268	26	9.7	1.33	0.82	2.15	0.2705
	≥38.5	256	21	8.2	268	13	4.9	1.69	0.88	3.27	0.1553
	≥39.0	256	12	4.7	268	3	1.1	4.19	1.29	13.72	0.0173
	≥40.0	256	2	0.8	268	0	0.0	INF	0.55	INF	0.2382
	Related	256	28	10.9	268	18	6.7	1.63	0.93	2.86	0.0919
	≥38 Related	256	25	9.8	268	18	6.7	1.45	0.82	2.58	0.2649
	≥38.5 Related	256	18	7.0	268	8	3.0	2.36	1.07	5.23	0.0430
	≥39.0 Related	256	10	3.9	268	3	1.1	3.49	1.05	11.68	0.0498
	≥40.0 Related	256	1	0.4	268	0	0.0	INF	0.27	INF	0.4885
Overall/subject											
Temperature/(Axillary) (°C)	All	135	34	25.2	141	23	16.3	1.54	0.97	2.48	0.0756
	≥38	135	31	23.0	141	23	16.3	1.41	0.87	2.28	0.1749
	≥38.5	135	19	14.1	141	12	8.5	1.65	0.85	3.25	0.1821
	≥39.0	135	12	8.9	141	3	2.1	4.18	1.30	13.61	0.0160
	≥40.0	135	2	1.5	141	0	0.0	INF	0.55	INF	0.2383
	Related	135	26	19.3	141	18	12.8	1.51	0.87	2.61	0.1878
	≥38 Related	135	23	17.0	141	18	12.8	1.33	0.76	2.35	0.3976
	≥38.5 Related	135	16	11.9	141	8	5.7	2.09	0.95	4.65	0.0873
	≥39.0 Related	135	10	7.4	141	3	2.1	3.48	1.06	11.58	0.0476
	≥40.0 Related	135	1	0.7	141	0	0.0	INF	0.27	INF	0.4891

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine

18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 165 Incidence of concomitant medication use during the 28-day (Days 0-27) post-vaccination period by dose and overall by age strata (Total vaccinated cohort)

	Q-QIV									
	6-17M					18-35M				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	157	61	38.9	31.2	46.9	142	58	40.8	32.7	49.4
Any antipyretic	157	34	21.7	15.5	28.9	142	33	23.2	16.6	31.1
Prophylactic antipyretic	157	5	3.2	1.0	7.3	142	4	2.8	0.8	7.1
Dose 2										
Any	155	51	32.9	25.6	40.9	122	40	32.8	24.6	41.9
Any antipyretic	155	28	18.1	12.4	25.0	122	19	15.6	9.6	23.2
Prophylactic antipyretic	155	0	0.0	0.0	2.4	122	0	0.0	0.0	3.0
Overall/dose										
Any	312	112	35.9	30.6	41.5	264	98	37.1	31.3	43.3
Any antipyretic	312	62	19.9	15.6	24.7	264	52	19.7	15.1	25.0
Prophylactic antipyretic	312	5	1.6	0.5	3.7	264	4	1.5	0.4	3.8
Overall/subject										
Any	157	80	51.0	42.9	59.0	142	77	54.2	45.7	62.6
Any antipyretic	157	50	31.8	24.6	39.7	142	45	31.7	24.1	40.0
Prophylactic antipyretic	157	5	3.2	1.0	7.3	142	4	2.8	0.8	7.1

	D-TIV-YB									
	6-17M					18-35M				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	160	80	50.0	42.0	58.0	142	50	35.2	27.4	43.7
Any antipyretic	160	45	28.1	21.3	35.8	142	28	19.7	13.5	27.2
Prophylactic antipyretic	160	4	2.5	0.7	6.3	142	1	0.7	0.0	3.9
Dose 2										
Any	154	55	35.7	28.2	43.8	127	43	33.9	25.7	42.8
Any antipyretic	154	33	21.4	15.2	28.8	127	13	10.2	5.6	16.9
Prophylactic antipyretic	154	2	1.3	0.2	4.6	127	1	0.8	0.0	4.3
Overall/dose										
Any	314	135	43.0	37.4	48.7	269	93	34.6	28.9	40.6
Any antipyretic	314	78	24.8	20.2	30.0	269	41	15.2	11.2	20.1
Prophylactic antipyretic	314	6	1.9	0.7	4.1	269	2	0.7	0.1	2.7
Overall/subject										
Any	160	97	60.6	52.6	68.2	142	72	50.7	42.2	59.2
Any antipyretic	160	65	40.6	32.9	48.7	142	34	23.9	17.2	31.8
Prophylactic antipyretic	160	6	3.8	1.4	8.0	142	2	1.4	0.2	5.0

	Total									
	6-17M					18-35M				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	317	141	44.5	38.9	50.1	284	108	38.0	32.4	44.0
Any antipyretic	317	79	24.9	20.3	30.1	284	61	21.5	16.8	26.7
Prophylactic antipyretic	317	9	2.8	1.3	5.3	284	5	1.8	0.6	4.1
Dose 2										
Any	309	106	34.3	29.0	39.9	249	83	33.3	27.5	39.6
Any antipyretic	309	61	19.7	15.5	24.6	249	32	12.9	9.0	17.7
Prophylactic antipyretic	309	2	0.6	0.1	2.3	249	1	0.4	0.0	2.2
Overall/dose										
Any	626	247	39.5	35.6	43.4	533	191	35.8	31.8	40.1
Any antipyretic	626	140	22.4	19.2	25.8	533	93	17.4	14.3	20.9
Prophylactic antipyretic	626	11	1.8	0.9	3.1	533	6	1.1	0.4	2.4
Overall/subject										
Any	317	177	55.8	50.2	61.4	284	149	52.5	46.5	58.4
Any antipyretic	317	115	36.3	31.0	41.8	284	79	27.8	22.7	33.4
Prophylactic antipyretic	317	11	3.5	1.7	6.1	284	6	2.1	0.8	4.5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
Total = Total
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

10.3.3. By priming status

Table 166 Number and percentage of subjects who received study vaccine dose(s) (By priming status - Total Vaccinated cohort)

	Q-QIV				D-TIV-YB			
	UNPRIM N = 286		PRIM N = 13		UNPRIM N = 287		PRIM N = 15	
Total number of doses received	n	%	n	%	n	%	n	%
1	9	3.1	13	100	6	2.1	15	100
2	277	96.9	0	0.0	281	97.9	0	0.0
Any	286	100	13	100	287	100	15	100

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = number of subjects in each group included in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose

Table 167 Compliance in returning symptom sheets (By priming status - Total Vaccinated cohort)

Dose	Group	Sub-group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
1	Q-QIV	UNPRIM	286	6	276	96.5	277	96.9
		PRIM	13	0	13	100	13	100
	D-TIV-YB	UNPRIM	287	8	281	97.9	282	98.3
		PRIM	15	0	15	100	15	100
2	Q-QIV	UNPRIM	277	0	272	98.2	274	98.9
	D-TIV-YB	UNPRIM	281	2	276	98.2	276	98.2
Total	Q-QIV	UNPRIM	563	6	548	97.3	551	97.9
		PRIM	13	0	13	100	13	100
	D-TIV-YB	UNPRIM	568	10	557	98.1	558	98.2
		PRIM	15	0	15	100	15	100

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
SS = Symptom sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom sheet return / number of administered doses) X 100

Table 168 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By priming status - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	148	51.7	45.8	57.7	286	140	49.0	43.0	54.9
		PRIM	13	11	84.6	54.6	98.1	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	287	158	55.1	49.1	60.9	287	141	49.1	43.2	55.1
		PRIM	15	11	73.3	44.9	92.2	15	11	73.3	44.9	92.2
Dose 2	Q-QIV	UNPRIM	277	126	45.5	39.5	51.6	277	112	40.4	34.6	46.5
	D-TIV-YB	UNPRIM	281	133	47.3	41.4	53.3	281	118	42.0	36.2	48.0
Overall/dose	Q-QIV	UNPRIM	563	274	48.7	44.5	52.9	563	252	44.8	40.6	49.0
		PRIM	13	11	84.6	54.6	98.1	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	568	291	51.2	47.0	55.4	568	259	45.6	41.4	49.8
		PRIM	15	11	73.3	44.9	92.2	15	11	73.3	44.9	92.2
Overall/subject	Q-QIV	UNPRIM	286	179	62.6	56.7	68.2	286	170	59.4	53.5	65.2
		PRIM	13	11	84.6	54.6	98.1	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	287	194	67.6	61.8	73.0	287	178	62.0	56.1	67.7
		PRIM	15	11	73.3	44.9	92.2	15	11	73.3	44.9	92.2

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	72	25.2	20.3	30.6
		PRIM	13	5	38.5	13.9	68.4
	D-TIV-YB	UNPRIM	287	64	22.3	17.6	27.6
		PRIM	15	4	26.7	7.8	55.1
Dose 2	Q-QIV	UNPRIM	277	58	20.9	16.3	26.2
	D-TIV-YB	UNPRIM	281	63	22.4	17.7	27.8
Overall/dose	Q-QIV	UNPRIM	563	130	23.1	19.7	26.8
		PRIM	13	5	38.5	13.9	68.4
	D-TIV-YB	UNPRIM	568	127	22.4	19.0	26.0
		PRIM	15	4	26.7	7.8	55.1
Overall/subject	Q-QIV	UNPRIM	286	93	32.5	27.1	38.3
		PRIM	13	5	38.5	13.9	68.4
	D-TIV-YB	UNPRIM	287	92	32.1	26.7	37.8
		PRIM	15	4	26.7	7.8	55.1

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 169 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By priming status - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	30	10.5	7.2	14.6	286	29	10.1	6.9	14.2
		PRIM	13	1	7.7	0.2	36.0	13	1	7.7	0.2	36.0
	D-TIV-YB	UNPRIM	287	22	7.7	4.9	11.4	287	22	7.7	4.9	11.4
		PRIM	15	0	0.0	0.0	21.8	15	0	0.0	0.0	21.8
Dose 2	Q-QIV	UNPRIM	277	24	8.7	5.6	12.6	277	23	8.3	5.3	12.2
	D-TIV-YB	UNPRIM	281	18	6.4	3.8	9.9	281	16	5.7	3.3	9.1
Overall/dose	Q-QIV	UNPRIM	563	54	9.6	7.3	12.3	563	52	9.2	7.0	11.9
		PRIM	13	1	7.7	0.2	36.0	13	1	7.7	0.2	36.0
	D-TIV-YB	UNPRIM	568	40	7.0	5.1	9.5	568	38	6.7	4.8	9.1
		PRIM	15	0	0.0	0.0	21.8	15	0	0.0	0.0	21.8
Overall/subject	Q-QIV	UNPRIM	286	46	16.1	12.0	20.9	286	45	15.7	11.7	20.5
		PRIM	13	1	7.7	0.2	36.0	13	1	7.7	0.2	36.0
	D-TIV-YB	UNPRIM	287	36	12.5	8.9	16.9	287	35	12.2	8.6	16.6
		PRIM	15	0	0.0	0.0	21.8	15	0	0.0	0.0	21.8

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	5	1.7	0.6	4.0
		PRIM	13	0	0.0	0.0	24.7
	D-TIV-YB	UNPRIM	287	1	0.3	0.0	1.9
		PRIM	15	0	0.0	0.0	21.8
Dose 2	Q-QIV	UNPRIM	277	3	1.1	0.2	3.1
	D-TIV-YB	UNPRIM	281	3	1.1	0.2	3.1
Overall/dose	Q-QIV	UNPRIM	563	8	1.4	0.6	2.8
		PRIM	13	0	0.0	0.0	24.7
	D-TIV-YB	UNPRIM	568	4	0.7	0.2	1.8
		PRIM	15	0	0.0	0.0	21.8
Overall/subject	Q-QIV	UNPRIM	286	7	2.4	1.0	5.0
		PRIM	13	0	0.0	0.0	24.7
	D-TIV-YB	UNPRIM	287	3	1.0	0.2	3.0
		PRIM	15	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 170 Incidence and nature of symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By priming status - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	132	46.2	40.3	52.1	286	115	40.2	34.5	46.1
		PRIM	13	11	84.6	54.6	98.1	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	287	132	46.0	40.1	51.9	287	107	37.3	31.7	43.2
		PRIM	15	9	60.0	32.3	83.7	15	8	53.3	26.6	78.7
Dose 2	Q-QIV	UNPRIM	277	110	39.7	33.9	45.7	277	89	32.1	26.7	38.0
	D-TIV-YB	UNPRIM	281	115	40.9	35.1	46.9	281	95	33.8	28.3	39.7
Overall/dose	Q-QIV	UNPRIM	563	242	43.0	38.9	47.2	563	204	36.2	32.3	40.4
		PRIM	13	11	84.6	54.6	98.1	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	568	247	43.5	39.4	47.7	568	202	35.6	31.6	39.7
		PRIM	15	9	60.0	32.3	83.7	15	8	53.3	26.6	78.7
Overall/subject	Q-QIV	UNPRIM	286	159	55.6	49.6	61.4	286	139	48.6	42.7	54.6
		PRIM	13	11	84.6	54.6	98.1	13	9	69.2	38.6	90.9
	D-TIV-YB	UNPRIM	287	166	57.8	51.9	63.6	287	144	50.2	44.2	56.1
		PRIM	15	9	60.0	32.3	83.7	15	8	53.3	26.6	78.7

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	72	25.2	20.3	30.6
		PRIM	13	5	38.5	13.9	68.4
	D-TIV-YB	UNPRIM	287	63	22.0	17.3	27.2
		PRIM	15	4	26.7	7.8	55.1
Dose 2	Q-QIV	UNPRIM	277	58	20.9	16.3	26.2
	D-TIV-YB	UNPRIM	281	62	22.1	17.4	27.4
Overall/dose	Q-QIV	UNPRIM	563	130	23.1	19.7	26.8
		PRIM	13	5	38.5	13.9	68.4
	D-TIV-YB	UNPRIM	568	125	22.0	18.7	25.6
		PRIM	15	4	26.7	7.8	55.1
Overall/subject	Q-QIV	UNPRIM	286	93	32.5	27.1	38.3
		PRIM	13	5	38.5	13.9	68.4
	D-TIV-YB	UNPRIM	287	90	31.4	26.0	37.1
		PRIM	15	4	26.7	7.8	55.1

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 171 Incidence and nature of grade 3 symptoms (solicited and unsolicited) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By priming status - Total Vaccinated cohort)

			Any symptom					General symptoms				
						95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	23	8.0	5.2	11.8	286	22	7.7	4.9	11.4
		PRIM	13	1	7.7	0.2	36.0	13	1	7.7	0.2	36.0
	D-TIV-YB	UNPRIM	287	15	5.2	3.0	8.5	287	15	5.2	3.0	8.5
		PRIM	15	0	0.0	0.0	21.8	15	0	0.0	0.0	21.8
Dose 2	Q-QIV	UNPRIM	277	18	6.5	3.9	10.1	277	17	6.1	3.6	9.6
	D-TIV-YB	UNPRIM	281	16	5.7	3.3	9.1	281	14	5.0	2.8	8.2
Overall/dose	Q-QIV	UNPRIM	563	41	7.3	5.3	9.7	563	39	6.9	5.0	9.3
		PRIM	13	1	7.7	0.2	36.0	13	1	7.7	0.2	36.0
	D-TIV-YB	UNPRIM	568	31	5.5	3.7	7.7	568	29	5.1	3.4	7.3
		PRIM	15	0	0.0	0.0	21.8	15	0	0.0	0.0	21.8
Overall/subject	Q-QIV	UNPRIM	286	36	12.6	9.0	17.0	286	35	12.2	8.7	16.6
		PRIM	13	1	7.7	0.2	36.0	13	1	7.7	0.2	36.0
	D-TIV-YB	UNPRIM	287	28	9.8	6.6	13.8	287	27	9.4	6.3	13.4
		PRIM	15	0	0.0	0.0	21.8	15	0	0.0	0.0	21.8

			Local symptoms				
						95% CI	
	Group	Sub-group	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	286	5	1.7	0.6	4.0
		PRIM	13	0	0.0	0.0	24.7
	D-TIV-YB	UNPRIM	287	1	0.3	0.0	1.9
		PRIM	15	0	0.0	0.0	21.8
Dose 2	Q-QIV	UNPRIM	277	3	1.1	0.2	3.1
	D-TIV-YB	UNPRIM	281	3	1.1	0.2	3.1
Overall/dose	Q-QIV	UNPRIM	563	8	1.4	0.6	2.8
		PRIM	13	0	0.0	0.0	24.7
	D-TIV-YB	UNPRIM	568	4	0.7	0.2	1.8
		PRIM	15	0	0.0	0.0	21.8
Overall/subject	Q-QIV	UNPRIM	286	7	2.4	1.0	5.0
		PRIM	13	0	0.0	0.0	24.7
	D-TIV-YB	UNPRIM	287	3	1.0	0.2	3.0
		PRIM	15	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 172 Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By priming status - Total Vaccinated cohort)

		Q-QIV										D-TIV-YB				
		UNPRIM					PRIM					UNPRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Pain	All	277	68	24.5	19.6	30.1	13	5	38.5	13.9	68.4	282	60	21.3	16.6	26.5
	Grade 2 or 3	277	15	5.4	3.1	8.8	13	1	7.7	0.2	36.0	282	6	2.1	0.8	4.6
	Grade 3	277	5	1.8	0.6	4.2	13	0	0.0	0.0	24.7	282	1	0.4	0.0	2.0
	Medical advice	277	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
Redness (mm)	All	277	3	1.1	0.2	3.1	13	0	0.0	0.0	24.7	282	2	0.7	0.1	2.5
	>50.0	277	1	0.4	0.0	2.0	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	>100	277	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	Medical advice	277	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
Swelling (mm)	All	277	2	0.7	0.1	2.6	13	0	0.0	0.0	24.7	282	2	0.7	0.1	2.5
	>50.0	277	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	>100	277	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	Medical advice	277	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
Dose 2																
Pain	All	274	57	20.8	16.2	26.1						276	59	21.4	16.7	26.7
	Grade 2 or 3	274	18	6.6	3.9	10.2						276	15	5.4	3.1	8.8
	Grade 3	274	3	1.1	0.2	3.2						276	3	1.1	0.2	3.1
	Medical advice	274	1	0.4	0.0	2.0						276	0	0.0	0.0	1.3
Redness (mm)	All	274	4	1.5	0.4	3.7						276	4	1.4	0.4	3.7
	>50.0	274	1	0.4	0.0	2.0						276	0	0.0	0.0	1.3
	>100	274	0	0.0	0.0	1.3						276	0	0.0	0.0	1.3
	Medical advice	274	1	0.4	0.0	2.0						276	0	0.0	0.0	1.3
Swelling (mm)	All	274	4	1.5	0.4	3.7						276	5	1.8	0.6	4.2
	>50.0	274	1	0.4	0.0	2.0						276	0	0.0	0.0	1.3
	>100	274	0	0.0	0.0	1.3						276	0	0.0	0.0	1.3
	Medical advice	274	1	0.4	0.0	2.0						276	0	0.0	0.0	1.3
Overall/dose																
Pain	All	551	125	22.7	19.3	26.4	13	5	38.5	13.9	68.4	558	119	21.3	18.0	25.0
	Grade 2 or 3	551	33	6.0	4.2	8.3	13	1	7.7	0.2	36.0	558	21	3.8	2.3	5.7
	Grade 3	551	8	1.5	0.6	2.8	13	0	0.0	0.0	24.7	558	4	0.7	0.2	1.8
	Medical advice	551	1	0.2	0.0	1.0	13	0	0.0	0.0	24.7	558	0	0.0	0.0	0.7
Redness (mm)	All	551	7	1.3	0.5	2.6	13	0	0.0	0.0	24.7	558	6	1.1	0.4	2.3
	>50.0	551	2	0.4	0.0	1.3	13	0	0.0	0.0	24.7	558	0	0.0	0.0	0.7
	>100	551	0	0.0	0.0	0.7	13	0	0.0	0.0	24.7	558	0	0.0	0.0	0.7
	Medical advice	551	1	0.2	0.0	1.0	13	0	0.0	0.0	24.7	558	0	0.0	0.0	0.7
Swelling (mm)	All	551	6	1.1	0.4	2.4	13	0	0.0	0.0	24.7	558	7	1.3	0.5	2.6
	>50.0	551	1	0.2	0.0	1.0	13	0	0.0	0.0	24.7	558	0	0.0	0.0	0.7
	>100	551	0	0.0	0.0	0.7	13	0	0.0	0.0	24.7	558	0	0.0	0.0	0.7
	Medical advice	551	1	0.2	0.0	1.0	13	0	0.0	0.0	24.7	558	0	0.0	0.0	0.7
Overall/subject																
Pain	All	278	90	32.4	26.9	38.2	13	5	38.5	13.9	68.4	282	87	30.9	25.5	36.6
	Grade 2 or 3	278	26	9.4	6.2	13.4	13	1	7.7	0.2	36.0	282	18	6.4	3.8	9.9
	Grade 3	278	7	2.5	1.0	5.1	13	0	0.0	0.0	24.7	282	3	1.1	0.2	3.1
	Medical advice	278	1	0.4	0.0	2.0	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
Redness (mm)	All	278	6	2.2	0.8	4.6	13	0	0.0	0.0	24.7	282	6	2.1	0.8	4.6
	>50.0	278	2	0.7	0.1	2.6	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	>100	278	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	Medical advice	278	1	0.4	0.0	2.0	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3

		Q-QIV										D-TIV-YB				
		UNPRIM					PRIM					UNPRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Swelling (mm)	All	278	5	1.8	0.6	4.1	13	0	0.0	0.0	24.7	282	6	2.1	0.8	4.6
	>50.0	278	1	0.4	0.0	2.0	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	>100	278	0	0.0	0.0	1.3	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3
	Medical advice	278	1	0.4	0.0	2.0	13	0	0.0	0.0	24.7	282	0	0.0	0.0	1.3

		D-TIV-YB					Total									
		PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1																
Pain	All	15	4	26.7	7.8	55.1	559	128	22.9	19.5	26.6	28	9	32.1	15.9	52.4
	Grade 2 or 3	15	1	6.7	0.2	31.9	559	21	3.8	2.3	5.7	28	2	7.1	0.9	23.5
	Grade 3	15	0	0.0	0.0	21.8	559	6	1.1	0.4	2.3	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	559	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
Redness (mm)	All	15	0	0.0	0.0	21.8	559	5	0.9	0.3	2.1	28	0	0.0	0.0	12.3
	>50.0	15	0	0.0	0.0	21.8	559	1	0.2	0.0	1.0	28	0	0.0	0.0	12.3
	>100	15	0	0.0	0.0	21.8	559	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	559	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
Swelling (mm)	All	15	0	0.0	0.0	21.8	559	4	0.7	0.2	1.8	28	0	0.0	0.0	12.3
	>50.0	15	0	0.0	0.0	21.8	559	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
	>100	15	0	0.0	0.0	21.8	559	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	559	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
Dose 2																
Pain	All						550	116	21.1	17.8	24.7					
	Grade 2 or 3						550	33	6.0	4.2	8.3					
	Grade 3						550	6	1.1	0.4	2.4					
	Medical advice						550	1	0.2	0.0	1.0					
Redness (mm)	All						550	8	1.5	0.6	2.8					
	>50.0						550	1	0.2	0.0	1.0					
	>100						550	0	0.0	0.0	0.7					
	Medical advice						550	1	0.2	0.0	1.0					
Swelling (mm)	All						550	9	1.6	0.8	3.1					
	>50.0						550	1	0.2	0.0	1.0					
	>100						550	0	0.0	0.0	0.7					
	Medical advice						550	1	0.2	0.0	1.0					
Overall/dose																
Pain	All	15	4	26.7	7.8	55.1	1109	244	22.0	19.6	24.6	28	9	32.1	15.9	52.4
	Grade 2 or 3	15	1	6.7	0.2	31.9	1109	54	4.9	3.7	6.3	28	2	7.1	0.9	23.5
	Grade 3	15	0	0.0	0.0	21.8	1109	12	1.1	0.6	1.9	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	1109	1	0.1	0.0	0.5	28	0	0.0	0.0	12.3
Redness (mm)	All	15	0	0.0	0.0	21.8	1109	13	1.2	0.6	2.0	28	0	0.0	0.0	12.3
	>50.0	15	0	0.0	0.0	21.8	1109	2	0.2	0.0	0.6	28	0	0.0	0.0	12.3
	>100	15	0	0.0	0.0	21.8	1109	0	0.0	0.0	0.3	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	1109	1	0.1	0.0	0.5	28	0	0.0	0.0	12.3
Swelling (mm)	All	15	0	0.0	0.0	21.8	1109	13	1.2	0.6	2.0	28	0	0.0	0.0	12.3
	>50.0	15	0	0.0	0.0	21.8	1109	1	0.1	0.0	0.5	28	0	0.0	0.0	12.3
	>100	15	0	0.0	0.0	21.8	1109	0	0.0	0.0	0.3	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	1109	1	0.1	0.0	0.5	28	0	0.0	0.0	12.3

		D-TIV-YB					Total									
		PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Overall/subject																
Pain	All	15	4	26.7	7.8	55.1	560	177	31.6	27.8	35.6	28	9	32.1	15.9	52.4
	Grade 2 or 3	15	1	6.7	0.2	31.9	560	44	7.9	5.8	10.4	28	2	7.1	0.9	23.5
	Grade 3	15	0	0.0	0.0	21.8	560	10	1.8	0.9	3.3	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	560	1	0.2	0.0	1.0	28	0	0.0	0.0	12.3
Redness (mm)	All	15	0	0.0	0.0	21.8	560	12	2.1	1.1	3.7	28	0	0.0	0.0	12.3
	>50.0	15	0	0.0	0.0	21.8	560	2	0.4	0.0	1.3	28	0	0.0	0.0	12.3
	>100	15	0	0.0	0.0	21.8	560	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	560	1	0.2	0.0	1.0	28	0	0.0	0.0	12.3
Swelling (mm)	All	15	0	0.0	0.0	21.8	560	11	2.0	1.0	3.5	28	0	0.0	0.0	12.3
	>50.0	15	0	0.0	0.0	21.8	560	1	0.2	0.0	1.0	28	0	0.0	0.0	12.3
	>100	15	0	0.0	0.0	21.8	560	0	0.0	0.0	0.7	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	560	1	0.2	0.0	1.0	28	0	0.0	0.0	12.3

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
Total : n/%= number/percentage of subjects/doses with at least one local symptom whatever the number of injections.
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 173 Incidence of solicited general symptoms (excluding fever) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By priming status - Total Vaccinated cohort)

		Q-QIV										D-TIV-YB				
		UNPRIM					PRIM					UNPRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Drowsiness	All	276	69	25.0	20.0	30.5	13	3	23.1	5.0	53.8	281	60	21.4	16.7	26.6
	Grade 2 or 3	276	26	9.4	6.2	13.5	13	0	0.0	0.0	24.7	281	18	6.4	3.8	9.9
	Grade 3	276	6	2.2	0.8	4.7	13	0	0.0	0.0	24.7	281	4	1.4	0.4	3.6
	Related	276	56	20.3	15.7	25.5	13	3	23.1	5.0	53.8	281	52	18.5	14.1	23.5
	Grade 2 or 3 Related	276	21	7.6	4.8	11.4	13	0	0.0	0.0	24.7	281	16	5.7	3.3	9.1
	Grade 3 Related	276	5	1.8	0.6	4.2	13	0	0.0	0.0	24.7	281	3	1.1	0.2	3.1
	Medical advice	276	9	3.3	1.5	6.1	13	0	0.0	0.0	24.7	281	2	0.7	0.1	2.5
Irritability / fussiness	All	276	87	31.5	26.1	37.4	13	4	30.8	9.1	61.4	281	89	31.7	26.3	37.5
	Grade 2 or 3	276	33	12.0	8.4	16.4	13	2	15.4	1.9	45.4	281	29	10.3	7.0	14.5
	Grade 3	276	11	4.0	2.0	7.0	13	0	0.0	0.0	24.7	281	10	3.6	1.7	6.4
	Related	276	76	27.5	22.4	33.2	13	4	30.8	9.1	61.4	281	73	26.0	21.0	31.5
	Grade 2 or 3 Related	276	27	9.8	6.5	13.9	13	2	15.4	1.9	45.4	281	23	8.2	5.3	12.0
	Grade 3 Related	276	9	3.3	1.5	6.1	13	0	0.0	0.0	24.7	281	8	2.8	1.2	5.5
	Medical advice	276	10	3.6	1.8	6.6	13	0	0.0	0.0	24.7	281	6	2.1	0.8	4.6

		Q-QIV										D-TIV-YB				
		UNPRIM					PRIM					UNPRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Loss of appetite	All	276	74	26.8	21.7	32.5	13	4	30.8	9.1	61.4	281	65	23.1	18.3	28.5
	Grade 2 or 3	276	31	11.2	7.8	15.6	13	1	7.7	0.2	36.0	281	21	7.5	4.7	11.2
	Grade 3	276	9	3.3	1.5	6.1	13	0	0.0	0.0	24.7	281	7	2.5	1.0	5.1
	Related	276	64	23.2	18.3	28.6	13	3	23.1	5.0	53.8	281	51	18.1	13.8	23.2
	Grade 2 or 3 Related	276	26	9.4	6.2	13.5	13	1	7.7	0.2	36.0	281	15	5.3	3.0	8.7
	Grade 3 Related	276	9	3.3	1.5	6.1	13	0	0.0	0.0	24.7	281	3	1.1	0.2	3.1
	Medical advice	276	8	2.9	1.3	5.6	13	0	0.0	0.0	24.7	281	5	1.8	0.6	4.1
Dose 2																
Drowsiness	All	272	49	18.0	13.6	23.1						276	44	15.9	11.8	20.8
	Grade 2 or 3	272	15	5.5	3.1	8.9						276	13	4.7	2.5	7.9
	Grade 3	272	3	1.1	0.2	3.2						276	5	1.8	0.6	4.2
	Related	272	42	15.4	11.4	20.3						276	42	15.2	11.2	20.0
	Grade 2 or 3 Related	272	11	4.0	2.0	7.1						276	12	4.3	2.3	7.5
	Grade 3 Related	272	2	0.7	0.1	2.6						276	5	1.8	0.6	4.2
	Medical advice	272	6	2.2	0.8	4.7						276	1	0.4	0.0	2.0
Irritability / fussiness	All	272	72	26.5	21.3	32.1						276	75	27.2	22.0	32.8
	Grade 2 or 3	272	26	9.6	6.3	13.7						276	28	10.1	6.8	14.3
	Grade 3	272	6	2.2	0.8	4.7						276	5	1.8	0.6	4.2
	Related	272	63	23.2	18.3	28.6						276	67	24.3	19.3	29.8
	Grade 2 or 3 Related	272	22	8.1	5.1	12.0						276	23	8.3	5.4	12.2
	Grade 3 Related	272	4	1.5	0.4	3.7						276	4	1.4	0.4	3.7
	Medical advice	272	6	2.2	0.8	4.7						276	1	0.4	0.0	2.0
Loss of appetite	All	272	48	17.6	13.3	22.7						276	55	19.9	15.4	25.1
	Grade 2 or 3	272	20	7.4	4.5	11.1						276	18	6.5	3.9	10.1
	Grade 3	272	8	2.9	1.3	5.7						276	8	2.9	1.3	5.6
	Related	272	40	14.7	10.7	19.5						276	46	16.7	12.5	21.6
	Grade 2 or 3 Related	272	17	6.3	3.7	9.8						276	16	5.8	3.3	9.2
	Grade 3 Related	272	8	2.9	1.3	5.7						276	8	2.9	1.3	5.6
	Medical advice	272	8	2.9	1.3	5.7						276	3	1.1	0.2	3.1
Overall/dose																
Drowsiness	All	548	118	21.5	18.2	25.2	13	3	23.1	5.0	53.8	557	104	18.7	15.5	22.2
	Grade 2 or 3	548	41	7.5	5.4	10.0	13	0	0.0	0.0	24.7	557	31	5.6	3.8	7.8
	Grade 3	548	9	1.6	0.8	3.1	13	0	0.0	0.0	24.7	557	9	1.6	0.7	3.0
	Related	548	98	17.9	14.8	21.4	13	3	23.1	5.0	53.8	557	94	16.9	13.9	20.3
	Grade 2 or 3 Related	548	32	5.8	4.0	8.1	13	0	0.0	0.0	24.7	557	28	5.0	3.4	7.2
	Grade 3 Related	548	7	1.3	0.5	2.6	13	0	0.0	0.0	24.7	557	8	1.4	0.6	2.8
	Medical advice	548	15	2.7	1.5	4.5	13	0	0.0	0.0	24.7	557	3	0.5	0.1	1.6
Irritability / fussiness	All	548	159	29.0	25.2	33.0	13	4	30.8	9.1	61.4	557	164	29.4	25.7	33.4
	Grade 2 or 3	548	59	10.8	8.3	13.7	13	2	15.4	1.9	45.4	557	57	10.2	7.8	13.1
	Grade 3	548	17	3.1	1.8	4.9	13	0	0.0	0.0	24.7	557	15	2.7	1.5	4.4
	Related	548	139	25.4	21.8	29.2	13	4	30.8	9.1	61.4	557	140	25.1	21.6	29.0
	Grade 2 or 3 Related	548	49	8.9	6.7	11.6	13	2	15.4	1.9	45.4	557	46	8.3	6.1	10.9
	Grade 3 Related	548	13	2.4	1.3	4.0	13	0	0.0	0.0	24.7	557	12	2.2	1.1	3.7
	Medical advice	548	16	2.9	1.7	4.7	13	0	0.0	0.0	24.7	557	7	1.3	0.5	2.6
Loss of appetite	All	548	122	22.3	18.8	26.0	13	4	30.8	9.1	61.4	557	120	21.5	18.2	25.2
	Grade 2 or 3	548	51	9.3	7.0	12.1	13	1	7.7	0.2	36.0	557	39	7.0	5.0	9.4
	Grade 3	548	17	3.1	1.8	4.9	13	0	0.0	0.0	24.7	557	15	2.7	1.5	4.4
	Related	548	104	19.0	15.8	22.5	13	3	23.1	5.0	53.8	557	97	17.4	14.4	20.8
	Grade 2 or 3 Related	548	43	7.8	5.7	10.4	13	1	7.7	0.2	36.0	557	31	5.6	3.8	7.8
	Grade 3 Related	548	17	3.1	1.8	4.9	13	0	0.0	0.0	24.7	557	11	2.0	1.0	3.5
	Medical advice	548	16	2.9	1.7	4.7	13	0	0.0	0.0	24.7	557	8	1.4	0.6	2.8

		Q-QIV										D-TIV-YB				
		UNPRIM					PRIM					UNPRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject																
Drowsiness	All	277	90	32.5	27.0	38.4	13	3	23.1	5.0	53.8	281	84	29.9	24.6	35.6
	Grade 2 or 3	277	34	12.3	8.7	16.7	13	0	0.0	0.0	24.7	281	27	9.6	6.4	13.7
	Grade 3	277	9	3.2	1.5	6.1	13	0	0.0	0.0	24.7	281	9	3.2	1.5	6.0
	Related	277	76	27.4	22.3	33.1	13	3	23.1	5.0	53.8	281	77	27.4	22.3	33.0
	Grade 2 or 3 Related	277	28	10.1	6.8	14.3	13	0	0.0	0.0	24.7	281	24	8.5	5.5	12.4
	Grade 3 Related	277	7	2.5	1.0	5.1	13	0	0.0	0.0	24.7	281	8	2.8	1.2	5.5
	Medical advice	277	13	4.7	2.5	7.9	13	0	0.0	0.0	24.7	281	3	1.1	0.2	3.1
Irritability / fussiness	All	277	114	41.2	35.3	47.2	13	4	30.8	9.1	61.4	281	118	42.0	36.2	48.0
	Grade 2 or 3	277	52	18.8	14.3	23.9	13	2	15.4	1.9	45.4	281	49	17.4	13.2	22.4
	Grade 3	277	15	5.4	3.1	8.8	13	0	0.0	0.0	24.7	281	14	5.0	2.8	8.2
	Related	277	100	36.1	30.4	42.1	13	4	30.8	9.1	61.4	281	103	36.7	31.0	42.6
	Grade 2 or 3 Related	277	44	15.9	11.8	20.7	13	2	15.4	1.9	45.4	281	38	13.5	9.8	18.1
	Grade 3 Related	277	12	4.3	2.3	7.4	13	0	0.0	0.0	24.7	281	11	3.9	2.0	6.9
	Medical advice	277	14	5.1	2.8	8.3	13	0	0.0	0.0	24.7	281	7	2.5	1.0	5.1
Loss of appetite	All	277	95	34.3	28.7	40.2	13	4	30.8	9.1	61.4	281	94	33.5	28.0	39.3
	Grade 2 or 3	277	42	15.2	11.2	19.9	13	1	7.7	0.2	36.0	281	33	11.7	8.2	16.1
	Grade 3	277	16	5.8	3.3	9.2	13	0	0.0	0.0	24.7	281	14	5.0	2.8	8.2
	Related	277	81	29.2	24.0	35.0	13	3	23.1	5.0	53.8	281	77	27.4	22.3	33.0
	Grade 2 or 3 Related	277	36	13.0	9.3	17.5	13	1	7.7	0.2	36.0	281	27	9.6	6.4	13.7
	Grade 3 Related	277	16	5.8	3.3	9.2	13	0	0.0	0.0	24.7	281	11	3.9	2.0	6.9
	Medical advice	277	14	5.1	2.8	8.3	13	0	0.0	0.0	24.7	281	8	2.8	1.2	5.5

		D-TIV-YB					Total									
		PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1																
Drowsiness	All	15	4	26.7	7.8	55.1	557	129	23.2	19.7	26.9	28	7	25.0	10.7	44.9
	Grade 2 or 3	15	0	0.0	0.0	21.8	557	44	7.9	5.8	10.5	28	0	0.0	0.0	12.3
	Grade 3	15	0	0.0	0.0	21.8	557	10	1.8	0.9	3.3	28	0	0.0	0.0	12.3
	Related	15	3	20.0	4.3	48.1	557	108	19.4	16.2	22.9	28	6	21.4	8.3	41.0
	Grade 2 or 3 Related	15	0	0.0	0.0	21.8	557	37	6.6	4.7	9.0	28	0	0.0	0.0	12.3
	Grade 3 Related	15	0	0.0	0.0	21.8	557	8	1.4	0.6	2.8	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	557	11	2.0	1.0	3.5	28	0	0.0	0.0	12.3
Irritability / fussiness	All	15	5	33.3	11.8	61.6	557	176	31.6	27.8	35.6	28	9	32.1	15.9	52.4
	Grade 2 or 3	15	2	13.3	1.7	40.5	557	62	11.1	8.6	14.0	28	4	14.3	4.0	32.7
	Grade 3	15	0	0.0	0.0	21.8	557	21	3.8	2.3	5.7	28	0	0.0	0.0	12.3
	Related	15	3	20.0	4.3	48.1	557	149	26.8	23.1	30.6	28	7	25.0	10.7	44.9
	Grade 2 or 3 Related	15	1	6.7	0.2	31.9	557	50	9.0	6.7	11.7	28	3	10.7	2.3	28.2
	Grade 3 Related	15	0	0.0	0.0	21.8	557	17	3.1	1.8	4.8	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	557	16	2.9	1.7	4.6	28	0	0.0	0.0	12.3
Loss of appetite	All	15	6	40.0	16.3	67.7	557	139	25.0	21.4	28.8	28	10	35.7	18.6	55.9
	Grade 2 or 3	15	0	0.0	0.0	21.8	557	52	9.3	7.1	12.1	28	1	3.6	0.1	18.3
	Grade 3	15	0	0.0	0.0	21.8	557	16	2.9	1.7	4.6	28	0	0.0	0.0	12.3
	Related	15	6	40.0	16.3	67.7	557	115	20.6	17.4	24.2	28	9	32.1	15.9	52.4
	Grade 2 or 3 Related	15	0	0.0	0.0	21.8	557	41	7.4	5.3	9.9	28	1	3.6	0.1	18.3
	Grade 3 Related	15	0	0.0	0.0	21.8	557	12	2.2	1.1	3.7	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	557	13	2.3	1.2	4.0	28	0	0.0	0.0	12.3

		D-TIV-YB					Total									
		PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 2																
Drowsiness	All						548	93	17.0	13.9	20.4					
	Grade 2 or 3						548	28	5.1	3.4	7.3					
	Grade 3						548	8	1.5	0.6	2.9					
	Related						548	84	15.3	12.4	18.6					
	Grade 2 or 3 Related						548	23	4.2	2.7	6.2					
	Grade 3 Related						548	7	1.3	0.5	2.6					
	Medical advice						548	7	1.3	0.5	2.6					
Irritability / fussiness	All						548	147	26.8	23.2	30.7					
	Grade 2 or 3						548	54	9.9	7.5	12.7					
	Grade 3						548	11	2.0	1.0	3.6					
	Related						548	130	23.7	20.2	27.5					
	Grade 2 or 3 Related						548	45	8.2	6.1	10.8					
	Grade 3 Related						548	8	1.5	0.6	2.9					
	Medical advice						548	7	1.3	0.5	2.6					
Loss of appetite	All						548	103	18.8	15.6	22.3					
	Grade 2 or 3						548	38	6.9	5.0	9.4					
	Grade 3						548	16	2.9	1.7	4.7					
	Related						548	86	15.7	12.7	19.0					
	Grade 2 or 3 Related						548	33	6.0	4.2	8.4					
	Grade 3 Related						548	16	2.9	1.7	4.7					
	Medical advice						548	11	2.0	1.0	3.6					
Overall/dose																
Drowsiness	All	15	4	26.7	7.8	55.1	1105	222	20.1	17.8	22.6	28	7	25.0	10.7	44.9
	Grade 2 or 3	15	0	0.0	0.0	21.8	1105	72	6.5	5.1	8.1	28	0	0.0	0.0	12.3
	Grade 3	15	0	0.0	0.0	21.8	1105	18	1.6	1.0	2.6	28	0	0.0	0.0	12.3
	Related	15	3	20.0	4.3	48.1	1105	192	17.4	15.2	19.7	28	6	21.4	8.3	41.0
	Grade 2 or 3 Related	15	0	0.0	0.0	21.8	1105	60	5.4	4.2	6.9	28	0	0.0	0.0	12.3
	Grade 3 Related	15	0	0.0	0.0	21.8	1105	15	1.4	0.8	2.2	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	1105	18	1.6	1.0	2.6	28	0	0.0	0.0	12.3
Irritability / fussiness	All	15	5	33.3	11.8	61.6	1105	323	29.2	26.6	32.0	28	9	32.1	15.9	52.4
	Grade 2 or 3	15	2	13.3	1.7	40.5	1105	116	10.5	8.8	12.5	28	4	14.3	4.0	32.7
	Grade 3	15	0	0.0	0.0	21.8	1105	32	2.9	2.0	4.1	28	0	0.0	0.0	12.3
	Related	15	3	20.0	4.3	48.1	1105	279	25.2	22.7	27.9	28	7	25.0	10.7	44.9
	Grade 2 or 3 Related	15	1	6.7	0.2	31.9	1105	95	8.6	7.0	10.4	28	3	10.7	2.3	28.2
	Grade 3 Related	15	0	0.0	0.0	21.8	1105	25	2.3	1.5	3.3	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	1105	23	2.1	1.3	3.1	28	0	0.0	0.0	12.3
Loss of appetite	All	15	6	40.0	16.3	67.7	1105	242	21.9	19.5	24.5	28	10	35.7	18.6	55.9
	Grade 2 or 3	15	0	0.0	0.0	21.8	1105	90	8.1	6.6	9.9	28	1	3.6	0.1	18.3
	Grade 3	15	0	0.0	0.0	21.8	1105	32	2.9	2.0	4.1	28	0	0.0	0.0	12.3
	Related	15	6	40.0	16.3	67.7	1105	201	18.2	16.0	20.6	28	9	32.1	15.9	52.4
	Grade 2 or 3 Related	15	0	0.0	0.0	21.8	1105	74	6.7	5.3	8.3	28	1	3.6	0.1	18.3
	Grade 3 Related	15	0	0.0	0.0	21.8	1105	28	2.5	1.7	3.6	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	1105	24	2.2	1.4	3.2	28	0	0.0	0.0	12.3
Overall/subject																
Drowsiness	All	15	4	26.7	7.8	55.1	558	174	31.2	27.4	35.2	28	7	25.0	10.7	44.9
	Grade 2 or 3	15	0	0.0	0.0	21.8	558	61	10.9	8.5	13.8	28	0	0.0	0.0	12.3
	Grade 3	15	0	0.0	0.0	21.8	558	18	3.2	1.9	5.1	28	0	0.0	0.0	12.3
	Related	15	3	20.0	4.3	48.1	558	153	27.4	23.8	31.3	28	6	21.4	8.3	41.0
	Grade 2 or 3 Related	15	0	0.0	0.0	21.8	558	52	9.3	7.0	12.0	28	0	0.0	0.0	12.3
	Grade 3 Related	15	0	0.0	0.0	21.8	558	15	2.7	1.5	4.4	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	558	16	2.9	1.6	4.6	28	0	0.0	0.0	12.3

		D-TIV-YB					Total									
		PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Irritability / fussiness	All	15	5	33.3	11.8	61.6	558	232	41.6	37.5	45.8	28	9	32.1	15.9	52.4
	Grade 2 or 3	15	2	13.3	1.7	40.5	558	101	18.1	15.0	21.6	28	4	14.3	4.0	32.7
	Grade 3	15	0	0.0	0.0	21.8	558	29	5.2	3.5	7.4	28	0	0.0	0.0	12.3
	Related	15	3	20.0	4.3	48.1	558	203	36.4	32.4	40.5	28	7	25.0	10.7	44.9
	Grade 2 or 3 Related	15	1	6.7	0.2	31.9	558	82	14.7	11.9	17.9	28	3	10.7	2.3	28.2
	Grade 3 Related	15	0	0.0	0.0	21.8	558	23	4.1	2.6	6.1	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	558	21	3.8	2.3	5.7	28	0	0.0	0.0	12.3
Loss of appetite	All	15	6	40.0	16.3	67.7	558	189	33.9	29.9	38.0	28	10	35.7	18.6	55.9
	Grade 2 or 3	15	0	0.0	0.0	21.8	558	75	13.4	10.7	16.6	28	1	3.6	0.1	18.3
	Grade 3	15	0	0.0	0.0	21.8	558	30	5.4	3.7	7.6	28	0	0.0	0.0	12.3
	Related	15	6	40.0	16.3	67.7	558	158	28.3	24.6	32.3	28	9	32.1	15.9	52.4
	Grade 2 or 3 Related	15	0	0.0	0.0	21.8	558	63	11.3	8.8	14.2	28	1	3.6	0.1	18.3
	Grade 3 Related	15	0	0.0	0.0	21.8	558	27	4.8	3.2	7.0	28	0	0.0	0.0	12.3
	Medical advice	15	0	0.0	0.0	21.8	558	22	3.9	2.5	5.9	28	0	0.0	0.0	12.3

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 174 Incidence of solicited symptoms (Fever) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (By priming status - Total Vaccinated cohort)

		Q-QIV										D-TIV-YB				
		UNPRIM					PRIM					UNPRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																
Temperature/(Axillary) (°C)	All	276	41	14.9	10.9	19.6	13	3	23.1	5.0	53.8	281	43	15.3	11.3	20.1
	≥38	276	39	14.1	10.2	18.8	13	3	23.1	5.0	53.8	281	42	14.9	11.0	19.7
	≥38.5	276	19	6.9	4.2	10.5	13	2	15.4	1.9	45.4	281	22	7.8	5.0	11.6
	≥39.0	276	10	3.6	1.8	6.6	13	1	7.7	0.2	36.0	281	9	3.2	1.5	6.0
	≥40.0	276	1	0.4	0.0	2.0	13	0	0.0	0.0	24.7	281	2	0.7	0.1	2.5
	Related	276	30	10.9	7.5	15.2	13	3	23.1	5.0	53.8	281	30	10.7	7.3	14.9
	≥38 Related	276	28	10.1	6.8	14.3	13	3	23.1	5.0	53.8	281	29	10.3	7.0	14.5
	≥38.5 Related	276	15	5.4	3.1	8.8	13	2	15.4	1.9	45.4	281	13	4.6	2.5	7.8
	≥39.0 Related	276	7	2.5	1.0	5.2	13	1	7.7	0.2	36.0	281	5	1.8	0.6	4.1
	≥40.0 Related	276	1	0.4	0.0	2.0	13	0	0.0	0.0	24.7	281	1	0.4	0.0	2.0
Dose 2																
Temperature/(Axillary) (°C)	All	272	31	11.4	7.9	15.8						276	25	9.1	5.9	13.1
	≥38	272	28	10.3	7.0	14.5						276	25	9.1	5.9	13.1
	≥38.5	272	22	8.1	5.1	12.0						276	13	4.7	2.5	7.9
	≥39.0	272	12	4.4	2.3	7.6						276	5	1.8	0.6	4.2
	≥40.0	272	2	0.7	0.1	2.6						276	1	0.4	0.0	2.0
	Related	272	24	8.8	5.7	12.8						276	21	7.6	4.8	11.4
	≥38 Related	272	22	8.1	5.1	12.0						276	21	7.6	4.8	11.4
	≥38.5 Related	272	18	6.6	4.0	10.3						276	10	3.6	1.8	6.6
	≥39.0 Related	272	9	3.3	1.5	6.2						276	4	1.4	0.4	3.7
	≥40.0 Related	272	1	0.4	0.0	2.0						276	1	0.4	0.0	2.0
Overall/dose																
Temperature/(Axillary) (°C)	All	548	72	13.1	10.4	16.3	13	3	23.1	5.0	53.8	557	68	12.2	9.6	15.2
	≥38	548	67	12.2	9.6	15.3	13	3	23.1	5.0	53.8	557	67	12.0	9.4	15.0
	≥38.5	548	41	7.5	5.4	10.0	13	2	15.4	1.9	45.4	557	35	6.3	4.4	8.6
	≥39.0	548	22	4.0	2.5	6.0	13	1	7.7	0.2	36.0	557	14	2.5	1.4	4.2
	≥40.0	548	3	0.5	0.1	1.6	13	0	0.0	0.0	24.7	557	3	0.5	0.1	1.6
	Related	548	54	9.9	7.5	12.7	13	3	23.1	5.0	53.8	557	51	9.2	6.9	11.9
	≥38 Related	548	50	9.1	6.8	11.9	13	3	23.1	5.0	53.8	557	50	9.0	6.7	11.7
	≥38.5 Related	548	33	6.0	4.2	8.4	13	2	15.4	1.9	45.4	557	23	4.1	2.6	6.1
	≥39.0 Related	548	16	2.9	1.7	4.7	13	1	7.7	0.2	36.0	557	9	1.6	0.7	3.0
	≥40.0 Related	548	2	0.4	0.0	1.3	13	0	0.0	0.0	24.7	557	2	0.4	0.0	1.3
Overall/subject																
Temperature/(Axillary) (°C)	All	277	63	22.7	17.9	28.1	13	3	23.1	5.0	53.8	281	60	21.4	16.7	26.6
	≥38	277	58	20.9	16.3	26.2	13	3	23.1	5.0	53.8	281	59	21.0	16.4	26.2
	≥38.5	277	38	13.7	9.9	18.3	13	2	15.4	1.9	45.4	281	33	11.7	8.2	16.1
	≥39.0	277	22	7.9	5.0	11.8	13	1	7.7	0.2	36.0	281	13	4.6	2.5	7.8
	≥40.0	277	3	1.1	0.2	3.1	13	0	0.0	0.0	24.7	281	3	1.1	0.2	3.1
	Related	277	46	16.6	12.4	21.5	13	3	23.1	5.0	53.8	281	47	16.7	12.6	21.6
	≥38 Related	277	42	15.2	11.2	19.9	13	3	23.1	5.0	53.8	281	46	16.4	12.2	21.2
	≥38.5 Related	277	30	10.8	7.4	15.1	13	2	15.4	1.9	45.4	281	23	8.2	5.3	12.0
	≥39.0 Related	277	16	5.8	3.3	9.2	13	1	7.7	0.2	36.0	281	9	3.2	1.5	6.0
	≥40.0 Related	277	2	0.7	0.1	2.6	13	0	0.0	0.0	24.7	281	2	0.7	0.1	2.5

		D-TIV-YB					Total									
		PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1																
Temperature/(Axillary) (°C)	All	15	1	6.7	0.2	31.9	557	84	15.1	12.2	18.3	28	4	14.3	4.0	32.7
	≥38	15	1	6.7	0.2	31.9	557	81	14.5	11.7	17.7	28	4	14.3	4.0	32.7
	≥38.5	15	0	0.0	0.0	21.8	557	41	7.4	5.3	9.9	28	2	7.1	0.9	23.5
	≥39.0	15	0	0.0	0.0	21.8	557	19	3.4	2.1	5.3	28	1	3.6	0.1	18.3
	≥40.0	15	0	0.0	0.0	21.8	557	3	0.5	0.1	1.6	28	0	0.0	0.0	12.3
	Related	15	1	6.7	0.2	31.9	557	60	10.8	8.3	13.6	28	4	14.3	4.0	32.7
	≥38 Related	15	1	6.7	0.2	31.9	557	57	10.2	7.8	13.1	28	4	14.3	4.0	32.7
	≥38.5 Related	15	0	0.0	0.0	21.8	557	28	5.0	3.4	7.2	28	2	7.1	0.9	23.5
	≥39.0 Related	15	0	0.0	0.0	21.8	557	12	2.2	1.1	3.7	28	1	3.6	0.1	18.3
	≥40.0 Related	15	0	0.0	0.0	21.8	557	2	0.4	0.0	1.3	28	0	0.0	0.0	12.3
Dose 2																
Temperature/(Axillary) (°C)	All						548	56	10.2	7.8	13.1					
	≥38						548	53	9.7	7.3	12.5					
	≥38.5						548	35	6.4	4.5	8.8					
	≥39.0						548	17	3.1	1.8	4.9					
	≥40.0						548	3	0.5	0.1	1.6					
	Related						548	45	8.2	6.1	10.8					
	≥38 Related						548	43	7.8	5.7	10.4					
	≥38.5 Related						548	28	5.1	3.4	7.3					
	≥39.0 Related						548	13	2.4	1.3	4.0					
	≥40.0 Related						548	2	0.4	0.0	1.3					
Overall/dose																
Temperature/(Axillary) (°C)	All	15	1	6.7	0.2	31.9	1105	140	12.7	10.8	14.8	28	4	14.3	4.0	32.7
	≥38	15	1	6.7	0.2	31.9	1105	134	12.1	10.3	14.2	28	4	14.3	4.0	32.7
	≥38.5	15	0	0.0	0.0	21.8	1105	76	6.9	5.5	8.5	28	2	7.1	0.9	23.5
	≥39.0	15	0	0.0	0.0	21.8	1105	36	3.3	2.3	4.5	28	1	3.6	0.1	18.3
	≥40.0	15	0	0.0	0.0	21.8	1105	6	0.5	0.2	1.2	28	0	0.0	0.0	12.3
	Related	15	1	6.7	0.2	31.9	1105	105	9.5	7.8	11.4	28	4	14.3	4.0	32.7
	≥38 Related	15	1	6.7	0.2	31.9	1105	100	9.0	7.4	10.9	28	4	14.3	4.0	32.7
	≥38.5 Related	15	0	0.0	0.0	21.8	1105	56	5.1	3.9	6.5	28	2	7.1	0.9	23.5
	≥39.0 Related	15	0	0.0	0.0	21.8	1105	25	2.3	1.5	3.3	28	1	3.6	0.1	18.3
	≥40.0 Related	15	0	0.0	0.0	21.8	1105	4	0.4	0.1	0.9	28	0	0.0	0.0	12.3
Overall/subject																
Temperature/(Axillary) (°C)	All	15	1	6.7	0.2	31.9	558	123	22.0	18.7	25.7	28	4	14.3	4.0	32.7
	≥38	15	1	6.7	0.2	31.9	558	117	21.0	17.7	24.6	28	4	14.3	4.0	32.7
	≥38.5	15	0	0.0	0.0	21.8	558	71	12.7	10.1	15.8	28	2	7.1	0.9	23.5
	≥39.0	15	0	0.0	0.0	21.8	558	35	6.3	4.4	8.6	28	1	3.6	0.1	18.3
	≥40.0	15	0	0.0	0.0	21.8	558	6	1.1	0.4	2.3	28	0	0.0	0.0	12.3
	Related	15	1	6.7	0.2	31.9	558	93	16.7	13.7	20.0	28	4	14.3	4.0	32.7
	≥38 Related	15	1	6.7	0.2	31.9	558	88	15.8	12.8	19.1	28	4	14.3	4.0	32.7
	≥38.5 Related	15	0	0.0	0.0	21.8	558	53	9.5	7.2	12.2	28	2	7.1	0.9	23.5
	≥39.0 Related	15	0	0.0	0.0	21.8	558	25	4.5	2.9	6.5	28	1	3.6	0.1	18.3
	≥40.0 Related	15	0	0.0	0.0	21.8	558	4	0.7	0.2	1.8	28	0	0.0	0.0	12.3

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
UNPRIM = Unprimed subjects; PRIM = Primed subjects
For each dose and overall/subject: N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting the symptom at least once
For Overall/dose: N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 175 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		135	47.2	41.3	53.2	7	53.8	25.1	80.8	158	55.1	49.1	60.9	7	46.7	21.3	73.4
---------- ( )	---------- ( )	0	0.0	0.0	1.3	0	0.0	0.0	24.7	2*	0.7	0.1	2.5	0	0.0	0.0	21.8
Ear and labyrinth disorders (10013993)	Ear haemorrhage (10014009)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Ear pain (10014020)	0	0.0	0.0	1.3	1	7.7	0.2	36.0	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Eye disorders (10015919)	Conjunctivitis (10010741)	2	0.7	0.1	2.5	1	7.7	0.2	36.0	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Lacrimation increased (10023644)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	0	0.0	0.0	1.3	1	6.7	0.2	31.9
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Diarrhoea (10012735)	37	12.9	9.3	17.4	1	7.7	0.2	36.0	37	12.9	9.2	17.3	1	6.7	0.2	31.9
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	1.3	1	7.7	0.2	36.0	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Enteritis (10014866)	0	0.0	0.0	1.3	1	7.7	0.2	36.0	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Faeces hard (10016101)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Flatulence (10016766)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	1	6.7	0.2	31.9
	Stomatitis (10042128)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Teething (10043183)	9	3.1	1.4	5.9	0	0.0	0.0	24.7	5	1.7	0.6	4.0	2	13.3	1.7	40.5
	Vomiting (10047700)	6	2.1	0.8	4.5	1	7.7	0.2	36.0	6	2.1	0.8	4.5	1	6.7	0.2	31.9
General disorders and administration site conditions (10018065)	Injection site erosion (10022059)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Injection site haematoma (10022066)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Injection site rash (10022094)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Irritability (10022998)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	4	1.4	0.4	3.5	0	0.0	0.0	21.8
	Pyrexia (10037660)	6	2.1	0.8	4.5	0	0.0	0.0	24.7	10	3.5	1.7	6.3	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Acute sinusitis (10001076)	4	1.4	0.4	3.5	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Acute tonsillitis (10001093)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Ascariasis (10003442)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Blastocystis infection (10005092)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Bronchiolitis (10006448)	4	1.4	0.4	3.5	0	0.0	0.0	24.7	4	1.4	0.4	3.5	0	0.0	0.0	21.8
	Bronchitis (10006451)	1	0.3	0.0	1.9	1	7.7	0.2	36.0	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Bronchopneumonia (10006469)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Bullous impetigo (10006563)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Cellulitis (10007882)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Croup infectious (10011416)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Cutaneous larva migrans (10059547)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Dengue fever (10012310)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Dysentery (10051402)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Ear infection (10014011)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	6	2.1	0.8	4.5	0	0.0	0.0	21.8
	Gastroenteritis (10017888)	12	4.2	2.2	7.2	0	0.0	0.0	24.7	7	2.4	1.0	5.0	0	0.0	0.0	21.8
	Gingivitis (10018292)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Impetigo (10021531)	3	1.0	0.2	3.0	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Infection parasitic (10021857)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Injection site cellulitis (10050057)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Laryngitis (10023874)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Lung infection (10061229)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	77	26.9	21.9	32.5	1	7.7	0.2	36.0	89	31.0	25.7	36.7	1	6.7	0.2	31.9
	Otitis media (10033078)	2	0.7	0.1	2.5	1	7.7	0.2	36.0	5	1.7	0.6	4.0	0	0.0	0.0	21.8
	Otitis media acute (10033079)	3	1.0	0.2	3.0	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Parasitic gastroenteritis (10067720)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Pharyngitis (10034835)	11	3.8	1.9	6.8	0	0.0	0.0	24.7	7	2.4	1.0	5.0	0	0.0	0.0	21.8
	Pharyngitis streptococcal (10034839)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Pneumonia (10035664)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Rhinitis (10039083)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	4	1.4	0.4	3.5	0	0.0	0.0	21.8
	Roseola (10039222)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Scarlet fever (10039587)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Sinusitis (10040753)	5	1.7	0.6	4.0	0	0.0	0.0	24.7	4	1.4	0.4	3.5	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Subcutaneous abscess (10042343)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Tinea pedis (10043873)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Tonsillitis (10044008)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Tooth abscess (10044016)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Upper respiratory tract infection (10046306)	6	2.1	0.8	4.5	1	7.7	0.2	36.0	9	3.1	1.4	5.9	1	6.7	0.2	31.9
	Viral infection (10047461)	4	1.4	0.4	3.5	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Viral upper respiratory tract infection (10047482)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	1	6.7	0.2	31.9
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Face injury (10050392)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Joint injury (10060820)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Lethargy (10024264)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Bronchial hyperreactivity (10066091)	5	1.7	0.6	4.0	0	0.0	0.0	24.7	5	1.7	0.6	4.0	0	0.0	0.0	21.8
	Cough (10011224)	10	3.5	1.7	6.3	3	23.1	5.0	53.8	5	1.7	0.6	4.0	0	0.0	0.0	21.8
	Nasal congestion (10028735)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Rhinitis allergic (10039085)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Rhinorrhoea (10039101)	1	0.3	0.0	1.9	1	7.7	0.2	36.0	3	1.0	0.2	3.0	1	6.7	0.2	31.9
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.3	0.0	1.9	1	7.7	0.2	36.0	0	0.0	0.0	1.3	1	6.7	0.2	31.9
	Dermatitis (10012431)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Dermatitis contact (10012442)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Dermatitis diaper (10012444)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Dermatosis (10048768)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Dry skin (10013786)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Ecchymosis (10014080)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Eczema (10014184)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Erythema (10015150)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Onychoclasis (10048886)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Prurigo (10037083)	3	1.0	0.2	3.0	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	1.3	1	7.7	0.2	36.0	3	1.0	0.2	3.0	1	6.7	0.2	31.9
	Rash generalised (10037858)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Swelling face (10042682)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Urticaria (10046735)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The 2 AEs for group Q-QIV indicated by "----------" correspond to AE descriptions = "FEVER" and "PARASISTISM" which were not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 176 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		186	33.0	29.2	37.1	7	53.8	25.1	80.8	202	35.6	31.6	39.7	7	46.7	21.3	73.4
---------- ( )	---------- ( )	0	0.0	0.0	0.7	0	0.0	0.0	24.7	2*	0.4	0.0	1.3	0	0.0	0.0	21.8
Ear and labyrinth disorders (10013993)	Ear haemorrhage (10014009)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Ear pain (10014020)	0	0.0	0.0	0.7	1	7.7	0.2	36.0	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Eye disorders (10015919)	Conjunctivitis (10010741)	2	0.4	0.0	1.3	1	7.7	0.2	36.0	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Lacrimation increased (10023644)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	0	0.0	0.0	0.6	1	6.7	0.2	31.9
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Diarrhoea (10012735)	42	7.5	5.4	10.0	1	7.7	0.2	36.0	41	7.2	5.2	9.7	1	6.7	0.2	31.9
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	0.7	1	7.7	0.2	36.0	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Enteritis (10014866)	0	0.0	0.0	0.7	1	7.7	0.2	36.0	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Faeces hard (10016101)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Flatulence (10016766)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	1	6.7	0.2	31.9
	Stomatitis (10042128)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Teething (10043183)	12	2.1	1.1	3.7	0	0.0	0.0	24.7	6	1.1	0.4	2.3	2	13.3	1.7	40.5
	Vomiting (10047700)	7	1.2	0.5	2.5	1	7.7	0.2	36.0	6	1.1	0.4	2.3	1	6.7	0.2	31.9
General disorders and administration site conditions (10018065)	Injection site erosion (10022059)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Injection site haematoma (10022066)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Injection site rash (10022094)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Irritability (10022998)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	4	0.7	0.2	1.8	0	0.0	0.0	21.8
	Pyrexia (10037660)	6	1.1	0.4	2.3	0	0.0	0.0	24.7	11	1.9	1.0	3.4	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Acute sinusitis (10001076)	4	0.7	0.2	1.8	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Acute tonsillitis (10001093)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Ascariasis (10003442)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Blastocystis infection (10005092)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Bronchiolitis (10006448)	4	0.7	0.2	1.8	0	0.0	0.0	24.7	4	0.7	0.2	1.8	0	0.0	0.0	21.8
	Bronchitis (10006451)	1	0.2	0.0	1.0	1	7.7	0.2	36.0	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Bronchopneumonia (10006469)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Bullous impetigo (10006563)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Cellulitis (10007882)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Croup infectious (10011416)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Cutaneous larva migrans (10059547)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Dengue fever (10012310)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Dysentery (10051402)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Ear infection (10014011)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	7	1.2	0.5	2.5	0	0.0	0.0	21.8
	Gastroenteritis (10017888)	12	2.1	1.1	3.7	0	0.0	0.0	24.7	7	1.2	0.5	2.5	0	0.0	0.0	21.8
	Gingivitis (10018292)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Impetigo (10021531)	3	0.5	0.1	1.5	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Infection parasitic (10021857)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Injection site cellulitis (10050057)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Laryngitis (10023874)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Lung infection (10061229)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	92	16.3	13.4	19.7	1	7.7	0.2	36.0	102	18.0	14.9	21.4	1	6.7	0.2	31.9
	Otitis media (10033078)	2	0.4	0.0	1.3	1	7.7	0.2	36.0	5	0.9	0.3	2.0	0	0.0	0.0	21.8
	Otitis media acute (10033079)	4	0.7	0.2	1.8	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Parasitic gastroenteritis (10067720)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Pharyngitis (10034835)	13	2.3	1.2	3.9	0	0.0	0.0	24.7	7	1.2	0.5	2.5	0	0.0	0.0	21.8
	Pharyngitis streptococcal (10034839)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Pneumonia (10035664)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Rhinitis (10039083)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	4	0.7	0.2	1.8	0	0.0	0.0	21.8
	Roseola (10039222)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Scarlet fever (10039587)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Sinusitis (10040753)	5	0.9	0.3	2.1	0	0.0	0.0	24.7	4	0.7	0.2	1.8	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Subcutaneous abscess (10042343)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Tinea pedis (10043873)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Tonsillitis (10044008)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Tooth abscess (10044016)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Upper respiratory tract infection (10046306)	7	1.2	0.5	2.5	1	7.7	0.2	36.0	10	1.8	0.8	3.2	1	6.7	0.2	31.9
	Viral infection (10047461)	5	0.9	0.3	2.1	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Viral upper respiratory tract infection (10047482)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	1	6.7	0.2	31.9
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Face injury (10050392)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Joint injury (10060820)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Lethargy (10024264)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Bronchial hyperreactivity (10066091)	5	0.9	0.3	2.1	0	0.0	0.0	24.7	5	0.9	0.3	2.0	0	0.0	0.0	21.8
	Cough (10011224)	11	2.0	1.0	3.5	3	23.1	5.0	53.8	6	1.1	0.4	2.3	0	0.0	0.0	21.8
	Nasal congestion (10028735)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Rhinitis allergic (10039085)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Rhinorrhoea (10039101)	1	0.2	0.0	1.0	1	7.7	0.2	36.0	3	0.5	0.1	1.5	1	6.7	0.2	31.9
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.2	0.0	1.0	1	7.7	0.2	36.0	0	0.0	0.0	0.6	1	6.7	0.2	31.9
	Dermatitis (10012431)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Dermatitis contact (10012442)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Dermatitis diaper (10012444)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Dermatosis (10048768)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Dry skin (10013786)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Ecchymosis (10014080)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Eczema (10014184)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Erythema (10015150)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Onychoclasis (10048886)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Prurigo (10037083)	3	0.5	0.1	1.5	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	0.7	1	7.7	0.2	36.0	3	0.5	0.1	1.5	1	6.7	0.2	31.9
	Rash generalised (10037858)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Swelling face (10042682)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Urticaria (10046735)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The 2 AEs for group Q-QIV indicated by "----------" correspond to AE descriptions = "FEVER" and "PARASISTISM" which were not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 177 Global Summary of unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
Number of subjects with at least one unsolicited symptom reported	135	7	158	7	293	14
Number of doses followed by at least one unsolicited symptom	186	7	202	7	388	14
Number of unsolicited symptoms classified by MedDRA Preferred Term*	279	16	307	12	586	28
Number of unsolicited symptoms reported**	291	17	315	12	606	29

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 178 Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		9	3.1	1.4	5.9	0	0.0	0.0	24.7	5	1.7	0.6	4.0	0	0.0	0.0	21.8
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Infections and infestations (10021881)	Croup infectious (10011416)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Ear infection (10014011)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Gastroenteritis (10017888)	4	1.4	0.4	3.5	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	3	1.0	0.2	3.0	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Otitis media acute (10033079)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Tonsillitis (10044008)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Skin and subcutaneous tissue disorders (10040785)	Erythema (10015150)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Urticaria (10046735)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 179 Percentage of doses with grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		10	1.8	0.9	3.2	0	0.0	0.0	24.7	5	0.9	0.3	2.0	0	0.0	0.0	21.8
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Infections and infestations (10021881)	Croup infectious (10011416)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Ear infection (10014011)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Gastroenteritis (10017888)	4	0.7	0.2	1.8	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	3	0.5	0.1	1.5	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Otitis media acute (10033079)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Tonsillitis (10044008)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Skin and subcutaneous tissue disorders (10040785)	Erythema (10015150)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Urticaria (10046735)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 180 Global Summary of grade 3 unsolicited adverse events reported within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
Number of subjects with at least one unsolicited symptom reported	9	0	5	0	14	0
Number of doses followed by at least one unsolicited symptom	10	0	5	0	15	0
Number of unsolicited symptoms classified by MedDRA Preferred Term*	12	0	7	0	19	0
Number of unsolicited symptoms reported**	13	0	7	0	20	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 181 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		15	5.2	3.0	8.5	2	15.4	1.9	45.4	10	3.5	1.7	6.3	3	20.0	4.3	48.1
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	4	1.4	0.4	3.5	1	7.7	0.2	36.0	3	1.0	0.2	3.0	1	6.7	0.2	31.9
	Faeces hard (10016101)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Vomiting (10047700)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	3	1.0	0.2	3.0	1	6.7	0.2	31.9
General disorders and administration site conditions (10018065)	Injection site rash (10022094)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Pyrexia (10037660)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Ear infection (10014011)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Injection site cellulitis (10050057)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	5	1.7	0.6	4.0	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Upper respiratory tract infection (10046306)	0	0.0	0.0	1.3	1	7.7	0.2	36.0	0	0.0	0.0	1.3	1	6.7	0.2	31.9
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.3	0.0	1.9	1	7.7	0.2	36.0	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Nasal congestion (10028735)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Rhinorrhoea (10039101)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Erythema (10015150)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	0	0.0	0.0	1.3	1	6.7	0.2	31.9

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects; PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 182 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		16	2.8	1.6	4.6	2	15.4	1.9	45.4	11	1.9	1.0	3.4	3	20.0	4.3	48.1
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	4	0.7	0.2	1.8	1	7.7	0.2	36.0	3	0.5	0.1	1.5	1	6.7	0.2	31.9
	Faeces hard (10016101)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Vomiting (10047700)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	3	0.5	0.1	1.5	1	6.7	0.2	31.9
General disorders and administration site conditions (10018065)	Injection site rash (10022094)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Pyrexia (10037660)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Ear infection (10014011)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Injection site cellulitis (10050057)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	5	0.9	0.3	2.1	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Upper respiratory tract infection (10046306)	0	0.0	0.0	0.7	1	7.7	0.2	36.0	0	0.0	0.0	0.6	1	6.7	0.2	31.9
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Psychiatric disorders (10037175)	Agitation (10001497)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.2	0.0	1.0	1	7.7	0.2	36.0	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Nasal congestion (10028735)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Rhinorrhoea (10039101)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Erythema (10015150)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	0	0.0	0.0	0.6	1	6.7	0.2	31.9

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects; PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 183 Global Summary of unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
Number of subjects with at least one unsolicited symptom reported	15	2	10	3	25	5
Number of doses followed by at least one unsolicited symptom	16	2	11	3	27	5
Number of unsolicited symptoms classified by MedDRA Preferred Term*	20	3	17	4	37	7
Number of unsolicited symptoms reported**	22	3	18	4	40	7

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 184 Percentage of subjects reporting the occurrence of grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Infections and infestations (10021881)	Nasopharyngitis (10028810)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 185 Percentage of doses with grade 3 unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Infections and infestations (10021881)	Nasopharyngitis (10028810)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 186 Global Summary of grade 3 unsolicited adverse events reported with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
Number of subjects with at least one unsolicited symptom reported	1	0	0	0	1	0
Number of doses followed by at least one unsolicited symptom	1	0	0	0	1	0
Number of unsolicited symptoms classified by MedDRA Preferred Term*	1	0	0	0	1	0
Number of unsolicited symptoms reported**	1	0	0	0	1	0

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 187 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		94	32.9	27.5	38.6	3	23.1	5.0	53.8	100	34.8	29.3	40.7	1	6.7	0.2	31.9
---------- ( )	---------- ( )	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1*	0.3	0.0	1.9	0	0.0	0.0	21.8
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Eye disorders (10015919)	Conjunctivitis (10010741)	1	0.3	0.0	1.9	1	7.7	0.2	36.0	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	18	6.3	3.8	9.8	0	0.0	0.0	24.7	22	7.7	4.9	11.4	0	0.0	0.0	21.8
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	1.3	1	7.7	0.2	36.0	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	0	0.0	0.0	1.3	1	6.7	0.2	31.9
	Stomatitis (10042128)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Vomiting (10047700)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	4	1.4	0.4	3.5	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Acute sinusitis (10001076)	4	1.4	0.4	3.5	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Acute tonsillitis (10001093)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Ascariasis (10003442)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Blastocystis infection (10005092)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Bronchiolitis (10006448)	4	1.4	0.4	3.5	0	0.0	0.0	24.7	4	1.4	0.4	3.5	0	0.0	0.0	21.8
	Bronchitis (10006451)	1	0.3	0.0	1.9	1	7.7	0.2	36.0	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Bronchopneumonia (10006469)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Bullous impetigo (10006563)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Cellulitis (10007882)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Croup infectious (10011416)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Cutaneous larva migrans (10059547)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Dengue fever (10012310)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Dysentery (10051402)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Ear infection (10014011)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	6	2.1	0.8	4.5	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Gastroenteritis (10017888)	8	2.8	1.2	5.4	0	0.0	0.0	24.7	5	1.7	0.6	4.0	0	0.0	0.0	21.8
	Gingivitis (10018292)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Impetigo (10021531)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Injection site cellulitis (10050057)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Laryngitis (10023874)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Lung infection (10061229)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	52	18.2	13.9	23.1	0	0.0	0.0	24.7	54	18.8	14.5	23.8	0	0.0	0.0	21.8
	Otitis media (10033078)	2	0.7	0.1	2.5	1	7.7	0.2	36.0	4	1.4	0.4	3.5	0	0.0	0.0	21.8
	Otitis media acute (10033079)	3	1.0	0.2	3.0	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Parasitic gastroenteritis (10067720)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Pharyngitis (10034835)	11	3.8	1.9	6.8	0	0.0	0.0	24.7	6	2.1	0.8	4.5	0	0.0	0.0	21.8
	Pharyngitis streptococcal (10034839)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Rhinitis (10039083)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	4	1.4	0.4	3.5	0	0.0	0.0	21.8
	Scarlet fever (10039587)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Sinusitis (10040753)	5	1.7	0.6	4.0	0	0.0	0.0	24.7	4	1.4	0.4	3.5	0	0.0	0.0	21.8
	Tinea pedis (10043873)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Tonsillitis (10044008)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Tooth abscess (10044016)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Upper respiratory tract infection (10046306)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Viral infection (10047461)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Face injury (10050392)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
	Joint injury (10060820)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	3	1.0	0.2	3.0	0	0.0	0.0	21.8
	Bronchial hyperreactivity (10066091)	5	1.7	0.6	4.0	0	0.0	0.0	24.7	5	1.7	0.6	4.0	0	0.0	0.0	21.8
	Cough (10011224)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Rhinitis allergic (10039085)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Dermatosis (10048768)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Eczema (10014184)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Onychoclasis (10048886)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Prurigo (10037083)	3	1.0	0.2	3.0	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
	Urticaria (10046735)	2	0.7	0.1	2.5	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" which was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 188 Percentage of doses with unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		116	20.6	17.3	24.2	3	23.1	5.0	53.8	110	19.4	16.2	22.9	1	6.7	0.2	31.9
---------- ( )	---------- ( )	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1*	0.2	0.0	1.0	0	0.0	0.0	21.8
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Eye disorders (10015919)	Conjunctivitis (10010741)	1	0.2	0.0	1.0	1	7.7	0.2	36.0	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	18	3.2	1.9	5.0	0	0.0	0.0	24.7	22	3.9	2.4	5.8	0	0.0	0.0	21.8
	Diarrhoea haemorrhagic (10012741)	0	0.0	0.0	0.7	1	7.7	0.2	36.0	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	0	0.0	0.0	0.6	1	6.7	0.2	31.9
	Stomatitis (10042128)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Vomiting (10047700)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	4	0.7	0.2	1.8	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Infections and infestations (10021881)	Abscess limb (10050473)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Acute sinusitis (10001076)	4	0.7	0.2	1.8	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Acute tonsillitis (10001093)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Ascariasis (10003442)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Blastocystis infection (10005092)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Bronchiolitis (10006448)	4	0.7	0.2	1.8	0	0.0	0.0	24.7	4	0.7	0.2	1.8	0	0.0	0.0	21.8
	Bronchitis (10006451)	1	0.2	0.0	1.0	1	7.7	0.2	36.0	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Bronchopneumonia (10006469)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Bullous impetigo (10006563)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Cellulitis (10007882)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Croup infectious (10011416)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Cutaneous larva migrans (10059547)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Dengue fever (10012310)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Dysentery (10051402)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Ear infection (10014011)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	7	1.2	0.5	2.5	0	0.0	0.0	21.8
	Gastroenteritis (10017888)	8	1.4	0.6	2.8	0	0.0	0.0	24.7	5	0.9	0.3	2.0	0	0.0	0.0	21.8
	Gingivitis (10018292)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Impetigo (10021531)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Injection site cellulitis (10050057)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Laryngitis (10023874)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Lung infection (10061229)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Nasopharyngitis (10028810)	57	10.1	7.8	12.9	0	0.0	0.0	24.7	56	9.9	7.5	12.6	0	0.0	0.0	21.8
	Otitis media (10033078)	2	0.4	0.0	1.3	1	7.7	0.2	36.0	4	0.7	0.2	1.8	0	0.0	0.0	21.8
	Otitis media acute (10033079)	3	0.5	0.1	1.5	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Parasitic gastroenteritis (10067720)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Pharyngitis (10034835)	13	2.3	1.2	3.9	0	0.0	0.0	24.7	6	1.1	0.4	2.3	0	0.0	0.0	21.8
	Pharyngitis streptococcal (10034839)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Rhinitis (10039083)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	4	0.7	0.2	1.8	0	0.0	0.0	21.8
	Scarlet fever (10039587)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Sinusitis (10040753)	5	0.9	0.3	2.1	0	0.0	0.0	24.7	4	0.7	0.2	1.8	0	0.0	0.0	21.8
	Tinea pedis (10043873)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Tonsillitis (10044008)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Tooth abscess (10044016)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Upper respiratory tract infection (10046306)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Viral infection (10047461)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Injury, poisoning and procedural complications (10022117)	Clavicle fracture (10009245)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Face injury (10050392)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
	Joint injury (10060820)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Reproductive system and breast disorders (10038604)	Balanitis (10004073)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Bronchial hyperreactivity (10066091)	5	0.9	0.3	2.1	0	0.0	0.0	24.7	5	0.9	0.3	2.0	0	0.0	0.0	21.8
	Cough (10011224)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rhinitis allergic (10039085)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Dermatosis (10048768)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Eczema (10014184)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Onychoclasis (10048886)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Prurigo (10037083)	3	0.5	0.1	1.5	0	0.0	0.0	24.7	3	0.5	0.1	1.5	0	0.0	0.0	21.8
	Rash (10037844)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
	Urticaria (10046735)	2	0.4	0.0	1.3	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Note: The AE for group Q-QIV indicated by "----------" corresponds to AE description = "PARASISTISM" which was not coded at the time of the database freeze for this analysis. The unsolicited symptoms tables generated for the Day 180 visit will include this coded information and will be reported in the Day 180 annex report.

Table 189 Global Summary of unsolicited adverse events reported with medically attended visit, within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
Number of subjects with at least one unsolicited symptom reported	94	3	100	1	194	4
Number of doses followed by at least one unsolicited symptom	116	3	110	1	226	4
Number of unsolicited symptoms classified by MedDRA Preferred Term*	159	4	167	1	326	5
Number of unsolicited symptoms reported**	162	4	167	1	329	5

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 190 Percentage of subjects reporting the occurrence of serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 286				PRIM N = 13				UNPRIM N = 287				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.3	0.0	1.9	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.3	0.0	1.9	0	0.0	0.0	24.7	0	0.0	0.0	1.3	0	0.0	0.0	21.8
Infections and infestations (10021881)	Blastocystis infection (10005092)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	1	0.3	0.0	1.9	0	0.0	0.0	21.8
	Bronchiolitis (10006448)	0	0.0	0.0	1.3	0	0.0	0.0	24.7	2	0.7	0.1	2.5	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects; PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the AE at least once
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 191 Percentage of doses with serious adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

		Q-QIV								D-TIV-YB							
		UNPRIM N = 563				PRIM N = 13				UNPRIM N = 568				PRIM N = 15			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.2	0.0	1.0	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.2	0.0	1.0	0	0.0	0.0	24.7	0	0.0	0.0	0.6	0	0.0	0.0	21.8
Infections and infestations (10021881)	Blastocystis infection (10005092)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	1	0.2	0.0	1.0	0	0.0	0.0	21.8
	Bronchiolitis (10006448)	0	0.0	0.0	0.7	0	0.0	0.0	24.7	2	0.4	0.0	1.3	0	0.0	0.0	21.8

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one AE experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 192 Global Summary of serious adverse events reported within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

	Group					
	Q-QIV		D-TIV-YB		All	
	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
Number of subjects with at least one unsolicited symptom reported	1	0	2	0	3	0
Number of doses followed by at least one unsolicited symptom	1	0	2	0	3	0
Number of unsolicited symptoms classified by MedDRA Preferred Term*	1	0	3	0	4	0
Number of unsolicited symptoms reported**	1	0	3	0	4	0

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects; PRIM = Primed subjects
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Table 193 Percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

No records exist in this table

Table 194 Listing of potential Immune-Mediated Disease reported within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

No records exist in this table

Table 195 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom during the 7-day post-vaccination period (By priming status - Total Vaccinated cohort)

								Relative Risk (Q-QIV/UNPRIM over D-TIV-YB/UNPRIM)			
		Q-QIV/UNPRIM			D-TIV-YB/UNPRIM				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Dose 1											
Drowsiness	All	276	69	25.0	281	60	21.4	1.17	0.87	1.59	0.3169
	Grade 3	276	6	2.2	281	4	1.4	1.53	0.47	5.00	0.5419
Irritability / fussiness	All	276	87	31.5	281	89	31.7	1.00	0.78	1.27	1.0000
	Grade 3	276	11	4.0	281	10	3.6	1.12	0.49	2.54	0.8273
Loss of appetite	All	276	74	26.8	281	65	23.1	1.16	0.87	1.55	0.3288
	Grade 3	276	9	3.3	281	7	2.5	1.31	0.51	3.35	0.6212
Dose 2											
Drowsiness	All	272	49	18.0	276	44	15.9	1.13	0.78	1.64	0.5698
	Grade 3	272	3	1.1	276	5	1.8	0.61	0.16	2.29	0.7246
Irritability / fussiness	All	272	72	26.5	276	75	27.2	0.97	0.74	1.28	0.9232
	Grade 3	272	6	2.2	276	5	1.8	1.22	0.40	3.72	0.7707
Loss of appetite	All	272	48	17.6	276	55	19.9	0.89	0.63	1.25	0.5133
	Grade 3	272	8	2.9	276	8	2.9	1.01	0.40	2.58	1.0000
Overall/dose											
Drowsiness	All	548	118	21.5	557	104	18.7	1.15	0.91	1.46	0.2601
	Grade 3	548	9	1.6	557	9	1.6	1.02	0.42	2.47	1.0000
Irritability / fussiness	All	548	159	29.0	557	164	29.4	0.99	0.82	1.18	0.8949
	Grade 3	548	17	3.1	557	15	2.7	1.15	0.59	2.26	0.7226
Loss of appetite	All	548	122	22.3	557	120	21.5	1.03	0.83	1.29	0.8273
	Grade 3	548	17	3.1	557	15	2.7	1.15	0.59	2.26	0.7226
Overall/subject											
Drowsiness	All	277	90	32.5	281	84	29.9	1.09	0.85	1.39	0.5234
	Grade 3	277	9	3.2	281	9	3.2	1.01	0.42	2.45	1.0000
Irritability / fussiness	All	277	114	41.2	281	118	42.0	0.98	0.80	1.19	0.8638
	Grade 3	277	15	5.4	281	14	5.0	1.09	0.54	2.18	0.8508
Loss of appetite	All	277	95	34.3	281	94	33.5	1.03	0.81	1.29	0.8583
	Grade 3	277	16	5.8	281	14	5.0	1.16	0.58	2.30	0.7109

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 196 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom during the 7-day post-vaccination period (By priming status - Total Vaccinated cohort)

								Relative Risk (Q-QIV/PRIM over D-TIV-YB/PRIM)			
		Q-QIV/PRIM			D-TIV-YB/PRIM				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Dose 1											
Drowsiness	All	13	3	23.1	15	4	26.7	0.87	0.24	2.98	1.0000
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Irritability / fussiness	All	13	4	30.8	15	5	33.3	0.92	0.31	2.66	1.0000
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Loss of appetite	All	13	4	30.8	15	6	40.0	0.77	0.27	2.07	0.7055
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/dose											
Drowsiness	All	13	3	23.1	15	4	26.7	0.87	0.24	2.98	1.0000
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Irritability / fussiness	All	13	4	30.8	15	5	33.3	0.92	0.31	2.66	1.0000
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Loss of appetite	All	13	4	30.8	15	6	40.0	0.77	0.27	2.07	0.7055
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/subject											
Drowsiness	All	13	3	23.1	15	4	26.7	0.87	0.24	2.98	1.0000
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Irritability / fussiness	All	13	4	30.8	15	5	33.3	0.92	0.31	2.66	1.0000
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Loss of appetite	All	13	4	30.8	15	6	40.0	0.77	0.27	2.07	0.7055
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 197 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited local symptom during the 7-day post-vaccination period (By priming status - Total Vaccinated cohort)

								Relative Risk (Q-QIV/UNPRIM over D-TIV-YB/UNPRIM)			
		Q-QIV/UNPRIM			D-TIV-YB/UNPRIM				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Dose 1											
Pain	All	277	68	24.5	282	60	21.3	1.15	0.85	1.57	0.3667
	Grade 3	277	5	1.8	282	1	0.4	5.09	0.79	32.80	0.1200
Redness (mm)	All	277	3	1.1	282	2	0.7	1.53	0.31	7.61	0.6836
	>100	277	0	0.0	282	0	0.0	INF	0.00	INF	
Swelling (mm)	All	277	2	0.7	282	2	0.7	1.02	0.18	5.75	1.0000
	>100	277	0	0.0	282	0	0.0	INF	0.00	INF	
Dose 2											
Pain	All	274	57	20.8	276	59	21.4	0.97	0.70	1.34	0.9169
	Grade 3	274	3	1.1	276	3	1.1	1.01	0.23	4.34	1.0000
Redness (mm)	All	274	4	1.5	276	4	1.4	1.01	0.28	3.65	1.0000
	>100	274	0	0.0	276	0	0.0	INF	0.00	INF	
Swelling (mm)	All	274	4	1.5	276	5	1.8	0.81	0.24	2.75	1.0000
	>100	274	0	0.0	276	0	0.0	INF	0.00	INF	
Overall/dose											
Pain	All	551	125	22.7	558	119	21.3	1.06	0.85	1.33	0.6121
	Grade 3	551	8	1.5	558	4	0.7	2.03	0.65	6.30	0.2615
Redness (mm)	All	551	7	1.3	558	6	1.1	1.18	0.42	3.33	0.7881
	>100	551	0	0.0	558	0	0.0	INF	0.00	INF	
Swelling (mm)	All	551	6	1.1	558	7	1.3	0.87	0.31	2.45	1.0000
	>100	551	0	0.0	558	0	0.0	INF	0.00	INF	
Overall/subject											
Pain	All	278	90	32.4	282	87	30.9	1.05	0.82	1.34	0.7168
	Grade 3	278	7	2.5	282	3	1.1	2.37	0.67	8.35	0.2195
Redness (mm)	All	278	6	2.2	282	6	2.1	1.01	0.35	2.95	1.0000
	>100	278	0	0.0	282	0	0.0	INF	0.00	INF	
Swelling (mm)	All	278	5	1.8	282	6	2.1	0.85	0.28	2.58	1.0000
	>100	278	0	0.0	282	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 198 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited local symptom during the 7-day post-vaccination period (By priming status - Total Vaccinated cohort)

								Relative Risk (Q-QIV/PRIM over D-TIV-YB/PRIM)			
		Q-QIV/PRIM			D-TIV-YB/PRIM				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Dose 1											
Pain	All	13	5	38.5	15	4	26.7	1.44	0.50	4.26	0.6891
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Redness (mm)	All	13	0	0.0	15	0	0.0	INF	0.00	INF	
	>100	13	0	0.0	15	0	0.0	INF	0.00	INF	
Swelling (mm)	All	13	0	0.0	15	0	0.0	INF	0.00	INF	
	>100	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/dose											
Pain	All	13	5	38.5	15	4	26.7	1.44	0.50	4.26	0.6891
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Redness (mm)	All	13	0	0.0	15	0	0.0	INF	0.00	INF	
	>100	13	0	0.0	15	0	0.0	INF	0.00	INF	
Swelling (mm)	All	13	0	0.0	15	0	0.0	INF	0.00	INF	
	>100	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/subject											
Pain	All	13	5	38.5	15	4	26.7	1.44	0.50	4.26	0.6891
	Grade 3	13	0	0.0	15	0	0.0	INF	0.00	INF	
Redness (mm)	All	13	0	0.0	15	0	0.0	INF	0.00	INF	
	>100	13	0	0.0	15	0	0.0	INF	0.00	INF	
Swelling (mm)	All	13	0	0.0	15	0	0.0	INF	0.00	INF	
	>100	13	0	0.0	15	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardised asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 199 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 48 hours of the vaccinations (By priming status UNPRIM-Total Vaccinated cohort)

								Relative Risk (Q-QIV/UNPRIM over D-TIV-YB/UNPRIM)			
		Q-QIV/UNPRIM			D-TIV-YB/UNPRIM				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	276	20	7.2	281	17	6.0	1.20	0.65	2.22	0.6125
	≥38	276	17	6.2	281	16	5.7	1.08	0.56	2.08	0.8590
	≥38.5	276	8	2.9	281	6	2.1	1.36	0.50	3.71	0.5997
	≥39.0	276	4	1.4	281	2	0.7	2.04	0.44	9.47	0.4469
	≥40.0	276	0	0.0	281	0	0.0	INF	0.00	INF	
	Related	276	19	6.9	281	16	5.7	1.21	0.64	2.28	0.6035
	≥38 Related	276	16	5.8	281	15	5.3	1.09	0.55	2.13	0.8549
	≥38.5 Related	276	7	2.5	281	5	1.8	1.43	0.48	4.21	0.5738
	≥39.0 Related	276	3	1.1	281	2	0.7	1.53	0.31	7.61	0.6836
	≥40.0 Related	276	0	0.0	281	0	0.0	INF	0.00	INF	
Dose 2											
Temperature/(Axillary) (°C)	All	272	16	5.9	276	12	4.3	1.35	0.66	2.77	0.4436
	≥38	272	16	5.9	276	12	4.3	1.35	0.66	2.77	0.4436
	≥38.5	272	10	3.7	276	2	0.7	5.07	1.26	20.51	0.0203
	≥39.0	272	5	1.8	276	1	0.4	5.07	0.79	32.69	0.1206
	≥40.0	272	0	0.0	276	0	0.0	INF	0.00	INF	
	Related	272	15	5.5	276	11	4.0	1.38	0.66	2.91	0.4280
	≥38 Related	272	15	5.5	276	11	4.0	1.38	0.66	2.91	0.4280
	≥38.5 Related	272	9	3.3	276	1	0.4	9.13	1.51	55.65	0.0106
	≥39.0 Related	272	4	1.5	276	0	0.0	INF	1.06	INF	0.0600
	≥40.0 Related	272	0	0.0	276	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	548	36	6.6	557	29	5.2	1.26	0.79	2.02	0.3718
	≥38	548	33	6.0	557	28	5.0	1.20	0.74	1.95	0.5113
	≥38.5	548	18	3.3	557	8	1.4	2.29	1.03	5.11	0.0479
	≥39.0	548	9	1.6	557	3	0.5	3.05	0.90	10.38	0.0882
	≥40.0	548	0	0.0	557	0	0.0	INF	0.00	INF	
	Related	548	34	6.2	557	27	4.8	1.28	0.79	2.08	0.3576
	≥38 Related	548	31	5.7	557	26	4.7	1.21	0.73	2.00	0.4979
	≥38.5 Related	548	16	2.9	557	6	1.1	2.71	1.10	6.68	0.0317
	≥39.0 Related	548	7	1.3	557	2	0.4	3.56	0.84	15.03	0.1053
	≥40.0 Related	548	0	0.0	557	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	277	31	11.2	281	28	10.0	1.12	0.70	1.81	0.6808
	≥38	277	28	10.1	281	27	9.6	1.05	0.64	1.73	0.8876
	≥38.5	277	17	6.1	281	8	2.8	2.16	0.97	4.82	0.0674
	≥39.0	277	9	3.2	281	3	1.1	3.04	0.90	10.33	0.0869
	≥40.0	277	0	0.0	281	0	0.0	INF	0.00	INF	
	Related	277	29	10.5	281	26	9.3	1.13	0.69	1.86	0.6715
	≥38 Related	277	26	9.4	281	25	8.9	1.06	0.63	1.77	0.8839
	≥38.5 Related	277	15	5.4	281	6	2.1	2.54	1.03	6.26	0.0468
	≥39.0 Related	277	7	2.5	281	2	0.7	3.55	0.85	14.97	0.1044
	≥40.0 Related	277	0	0.0	281	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
UNPRIM = Unprimed subjects

For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 200 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 48 hours of the vaccinations (By priming status PRIM- Total Vaccinated cohort)

								Relative Risk (Q-QIV/PRIM over D-TIV-YB/PRIM)			
		Q-QIV/PRIM			D-TIV-YB/PRIM				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38.5	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38 Related	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38.5 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38.5	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38 Related	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38.5 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38.5	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38 Related	13	2	15.4	15	1	6.7	2.31	0.32	17.04	0.5833
	≥38.5 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine; PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 201 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 4 days post-vaccinations (By priming status UNPRIM - Total Vaccinated cohort)

								Relative Risk (Q-QIV/UNPRIM over D-TIV-YB/UNPRIM)			
		Q-QIV/UNPRIM			D-TIV-YB/UNPRIM				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	276	30	10.9	281	28	10.0	1.09	0.67	1.77	0.7821
	≥38	276	29	10.5	281	25	8.9	1.18	0.71	1.96	0.5681
	≥38.5	276	14	5.1	281	11	3.9	1.30	0.61	2.76	0.5450
	≥39.0	276	6	2.2	281	4	1.4	1.53	0.47	5.00	0.5419
	≥40.0	276	0	0.0	281	1	0.4	0.00	0.00	3.91	1.0000
	Related	276	25	9.1	281	23	8.2	1.11	0.65	1.89	0.7638
	≥38 Related	276	24	8.7	281	21	7.5	1.16	0.67	2.03	0.6427
	≥38.5 Related	276	12	4.3	281	8	2.8	1.53	0.65	3.59	0.3709
	≥39.0 Related	276	4	1.4	281	3	1.1	1.36	0.34	5.39	0.7227
	≥40.0 Related	276	0	0.0	281	1	0.4	0.00	0.00	3.91	1.0000
Dose 2											
Temperature/(Axillary) (°C)	All	272	22	8.1	276	18	6.5	1.24	0.69	2.24	0.5145
	≥38	272	21	7.7	276	18	6.5	1.18	0.65	2.16	0.6211
	≥38.5	272	16	5.9	276	10	3.6	1.62	0.76	3.46	0.2335
	≥39.0	272	10	3.7	276	4	1.4	2.54	0.85	7.58	0.1115
	≥40.0	272	1	0.4	276	1	0.4	1.01	0.11	9.70	1.0000
	Related	272	17	6.3	276	15	5.4	1.15	0.59	2.23	0.7187
	≥38 Related	272	17	6.3	276	15	5.4	1.15	0.59	2.23	0.7187
	≥38.5 Related	272	13	4.8	276	7	2.5	1.88	0.79	4.53	0.1784
	≥39.0 Related	272	8	2.9	276	3	1.1	2.71	0.79	9.34	0.1395
	≥40.0 Related	272	0	0.0	276	1	0.4	0.00	0.00	3.89	1.0000
Overall/dose											
Temperature/(Axillary) (°C)	All	548	52	9.5	557	46	8.3	1.15	0.79	1.68	0.5257
	≥38	548	50	9.1	557	43	7.7	1.18	0.80	1.74	0.4484
	≥38.5	548	30	5.5	557	21	3.8	1.45	0.85	2.49	0.1980
	≥39.0	548	16	2.9	557	8	1.4	2.03	0.90	4.61	0.1015
	≥40.0	548	1	0.2	557	2	0.4	0.51	0.07	3.87	1.0000
	Related	548	42	7.7	557	38	6.8	1.12	0.74	1.71	0.6429
	≥38 Related	548	41	7.5	557	36	6.5	1.16	0.75	1.78	0.5553
	≥38.5 Related	548	25	4.6	557	15	2.7	1.69	0.91	3.15	0.1083
	≥39.0 Related	548	12	2.2	557	6	1.1	2.03	0.80	5.20	0.1605
	≥40.0 Related	548	0	0.0	557	2	0.4	0.00	0.00	1.95	0.4996
Overall/subject											
Temperature/(Axillary) (°C)	All	277	45	16.2	281	44	15.7	1.04	0.71	1.52	0.9081
	≥38	277	43	15.5	281	41	14.6	1.06	0.72	1.58	0.8132
	≥38.5	277	27	9.7	281	20	7.1	1.37	0.79	2.37	0.2883
	≥39.0	277	16	5.8	281	8	2.8	2.03	0.90	4.57	0.0982
	≥40.0	277	1	0.4	281	2	0.7	0.51	0.07	3.86	1.0000
	Related	277	36	13.0	281	37	13.2	0.99	0.65	1.51	1.0000
	≥38 Related	277	35	12.6	281	35	12.5	1.01	0.66	1.57	1.0000
	≥38.5 Related	277	22	7.9	281	15	5.3	1.49	0.80	2.78	0.2369
	≥39.0 Related	277	12	4.3	281	6	2.1	2.03	0.80	5.16	0.1576
	≥40.0 Related	277	0	0.0	281	2	0.7	0.00	0.00	1.94	0.4991

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine

UNPRIM = Unprimed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 202 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 4 days post-vaccinations (By priming status PRIM - Total Vaccinated cohort)

								Relative Risk (Q-QIV/PRIM over D-TIV-YB/PRIM)			
		Q-QIV/PRIM			D-TIV-YB/PRIM				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38 Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38 Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38 Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥39.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 203 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 7 days post-vaccinations (By priming status UNPRIM- Total Vaccinated cohort)

								Relative Risk (Q-QIV/UNPRIM over D-TIV-YB/UNPRIM)			
		Q-QIV/UNPRIM			D-TIV-YB/UNPRIM				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	276	41	14.9	281	43	15.3	0.97	0.66	1.44	0.9062
	≥38	276	39	14.1	281	42	14.9	0.95	0.63	1.41	0.8109
	≥38.5	276	19	6.9	281	22	7.8	0.88	0.49	1.57	0.7464
	≥39.0	276	10	3.6	281	9	3.2	1.13	0.48	2.67	0.8194
	≥40.0	276	1	0.4	281	2	0.7	0.51	0.07	3.87	1.0000
	Related	276	30	10.9	281	30	10.7	1.02	0.63	1.64	1.0000
	≥38 Related	276	28	10.1	281	29	10.3	0.98	0.60	1.60	1.0000
	≥38.5 Related	276	15	5.4	281	13	4.6	1.17	0.58	2.39	0.7017
	≥39.0 Related	276	7	2.5	281	5	1.8	1.43	0.48	4.21	0.5738
	≥40.0 Related	276	1	0.4	281	1	0.4	1.02	0.11	9.74	1.0000
Dose 2											
Temperature/(Axillary) (°C)	All	272	31	11.4	276	25	9.1	1.26	0.77	2.07	0.3992
	≥38	272	28	10.3	276	25	9.1	1.14	0.68	1.89	0.6661
	≥38.5	272	22	8.1	276	13	4.7	1.72	0.89	3.31	0.1179
	≥39.0	272	12	4.4	276	5	1.8	2.44	0.91	6.57	0.0892
	≥40.0	272	2	0.7	276	1	0.4	2.03	0.27	15.46	0.6216
	Related	272	24	8.8	276	21	7.6	1.16	0.67	2.02	0.6428
	≥38 Related	272	22	8.1	276	21	7.6	1.06	0.60	1.87	0.8747
	≥38.5 Related	272	18	6.6	276	10	3.6	1.83	0.87	3.83	0.1237
	≥39.0 Related	272	9	3.3	276	4	1.4	2.28	0.75	6.93	0.1717
	≥40.0 Related	272	1	0.4	276	1	0.4	1.01	0.11	9.70	1.0000
Overall/dose											
Temperature/(Axillary) (°C)	All	548	72	13.1	557	68	12.2	1.08	0.79	1.47	0.6522
	≥38	548	67	12.2	557	67	12.0	1.02	0.74	1.39	0.9269
	≥38.5	548	41	7.5	557	35	6.3	1.19	0.77	1.83	0.4764
	≥39.0	548	22	4.0	557	14	2.5	1.60	0.84	3.06	0.1775
	≥40.0	548	3	0.5	557	3	0.5	1.02	0.24	4.39	1.0000
	Related	548	54	9.9	557	51	9.2	1.08	0.75	1.55	0.7584
	≥38 Related	548	50	9.1	557	50	9.0	1.02	0.70	1.47	1.0000
	≥38.5 Related	548	33	6.0	557	23	4.1	1.46	0.87	2.44	0.1709
	≥39.0 Related	548	16	2.9	557	9	1.6	1.81	0.82	3.98	0.1608
	≥40.0 Related	548	2	0.4	557	2	0.4	1.02	0.18	5.75	1.0000
Overall/subject											
Temperature/(Axillary) (°C)	All	277	63	22.7	281	60	21.4	1.07	0.78	1.45	0.7594
	≥38	277	58	20.9	281	59	21.0	1.00	0.72	1.38	1.0000
	≥38.5	277	38	13.7	281	33	11.7	1.17	0.76	1.80	0.5263
	≥39.0	277	22	7.9	281	13	4.6	1.72	0.89	3.31	0.1181
	≥40.0	277	3	1.1	281	3	1.1	1.01	0.24	4.37	1.0000
	Related	277	46	16.6	281	47	16.7	0.99	0.69	1.44	1.0000
	≥38 Related	277	42	15.2	281	46	16.4	0.93	0.63	1.36	0.7284
	≥38.5 Related	277	30	10.8	281	23	8.2	1.32	0.79	2.21	0.3140
	≥39.0 Related	277	16	5.8	281	9	3.2	1.80	0.83	3.94	0.1565
	≥40.0 Related	277	2	0.7	281	2	0.7	1.01	0.18	5.73	1.0000

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine
UNPRIM = Unprimed subjects

For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 204 Difference between groups (Q-QIV over D-TIV-YB) in percentage of subjects reporting a specified solicited general symptom (Fever) within 7 days post-vaccinations (By priming status PRIM- Total Vaccinated cohort)

								Relative Risk (Q-QIV/PRIM over D-TIV-YB/PRIM)			
		Q-QIV/PRIM			D-TIV-YB/PRIM				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Temperature/(Axillary) (°C)	All	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5	13	2	15.4	15	0	0.0	INF	0.63	INF	0.2063
	≥39.0	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38 Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5 Related	13	2	15.4	15	0	0.0	INF	0.63	INF	0.2063
	≥39.0 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/dose											
Temperature/(Axillary) (°C)	All	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5	13	2	15.4	15	0	0.0	INF	0.63	INF	0.2063
	≥39.0	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38 Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5 Related	13	2	15.4	15	0	0.0	INF	0.63	INF	0.2063
	≥39.0 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	
Overall/subject											
Temperature/(Axillary) (°C)	All	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5	13	2	15.4	15	0	0.0	INF	0.63	INF	0.2063
	≥39.0	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥40.0	13	0	0.0	15	0	0.0	INF	0.00	INF	
	Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38 Related	13	3	23.1	15	1	6.7	3.46	0.55	23.36	0.3111
	≥38.5 Related	13	2	15.4	15	0	0.0	INF	0.63	INF	0.2063
	≥39.0 Related	13	1	7.7	15	0	0.0	INF	0.31	INF	0.4643
	≥40.0 Related	13	0	0.0	15	0	0.0	INF	0.00	INF	

Q-QIV = Flu Q-QIV Vaccine; D-TIV-YB = Fluarix Vaccine; PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval , LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test

Table 205 Incidence of concomitant medication use during the 28-day (Days 0-27) post-vaccination period by dose and overall by priming status (Total Vaccinated cohort)

	Q-QIV									
	UNPRIMED					PRIM				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	286	111	38.8	33.1	44.7	13	8	61.5	31.6	86.1
Any antipyretic	286	62	21.7	17.0	26.9	13	5	38.5	13.9	68.4
Prophylactic antipyretic	286	9	3.1	1.4	5.9	13	0	0.0	0.0	24.7
Dose 2										
Any	277	91	32.9	27.4	38.7	0	0			
Any antipyretic	277	47	17.0	12.7	21.9	0	0			
Prophylactic antipyretic	277	0	0.0	0.0	1.3	0	0			
Overall/dose										
Any	563	202	35.9	31.9	40.0	13	8	61.5	31.6	86.1
Any antipyretic	563	109	19.4	16.2	22.9	13	5	38.5	13.9	68.4
Prophylactic antipyretic	563	9	1.6	0.7	3.0	13	0	0.0	0.0	24.7
Overall/subject										
Any	286	149	52.1	46.1	58.0	13	8	61.5	31.6	86.1
Any antipyretic	286	90	31.5	26.1	37.2	13	5	38.5	13.9	68.4
Prophylactic antipyretic	286	9	3.1	1.4	5.9	13	0	0.0	0.0	24.7

	D-TIV-YB									
	UNPRIMED					PRIM				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	287	121	42.2	36.4	48.1	15	9	60.0	32.3	83.7
Any antipyretic	287	68	23.7	18.9	29.0	15	5	33.3	11.8	61.6
Prophylactic antipyretic	287	5	1.7	0.6	4.0	15	0	0.0	0.0	21.8
Dose 2										
Any	281	98	34.9	29.3	40.8	0	0			
Any antipyretic	281	46	16.4	12.2	21.2	0	0			
Prophylactic antipyretic	281	3	1.1	0.2	3.1	0	0			
Overall/dose										
Any	568	219	38.6	34.5	42.7	15	9	60.0	32.3	83.7
Any antipyretic	568	114	20.1	16.9	23.6	15	5	33.3	11.8	61.6
Prophylactic antipyretic	568	8	1.4	0.6	2.8	15	0	0.0	0.0	21.8
Overall/subject										
Any	287	160	55.7	49.8	61.6	15	9	60.0	32.3	83.7
Any antipyretic	287	94	32.8	27.4	38.5	15	5	33.3	11.8	61.6
Prophylactic antipyretic	287	8	2.8	1.2	5.4	15	0	0.0	0.0	21.8

	Total									
	UNPRIMED					PRIM				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	573	232	40.5	36.4	44.6	28	17	60.7	40.6	78.5
Any antipyretic	573	130	22.7	19.3	26.3	28	10	35.7	18.6	55.9
Prophylactic antipyretic	573	14	2.4	1.3	4.1	28	0	0.0	0.0	12.3
Dose 2										
Any	558	189	33.9	29.9	38.0	0	0			
Any antipyretic	558	93	16.7	13.7	20.0	0	0			
Prophylactic antipyretic	558	3	0.5	0.1	1.6	0	0			
Overall/dose										
Any	1131	421	37.2	34.4	40.1	28	17	60.7	40.6	78.5
Any antipyretic	1131	223	19.7	17.4	22.2	28	10	35.7	18.6	55.9
Prophylactic antipyretic	1131	17	1.5	0.9	2.4	28	0	0.0	0.0	12.3
Overall/subject										
Any	573	309	53.9	49.7	58.1	28	17	60.7	40.6	78.5
Any antipyretic	573	184	32.1	28.3	36.1	28	10	35.7	18.6	55.9
Prophylactic antipyretic	573	17	3.0	1.7	4.7	28	0	0.0	0.0	12.3

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = Fluarix Vaccine
Total = Total
UNPRIMED = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

11. REFERENCES

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12. STUDY REPORT AUTHORS /CONTRIBUTING AUTHORS

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Company, contractor for GSK Biologicals

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Clinical Regulatory Affairs: (b) (6)

N + 1 equivalent of CDM: (b) (6), MD

13. SERIOUS ADVERSE EVENTS / OTHER SIGNIFICANT ADVERSE EVENTS

13.1. SAE Listings

Table 206 Listing of SAEs reported within the 28-day (Days 0-27) post-vaccination period (Total Vaccinated cohort)

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
Q-QIV	(b) (6)		16	M	Acute diahrrea	Diarrhoea	Gastrointestinal disorders	HO	2	3	7	2	N	Recovered / resolved
D-TIV-YB			13	M	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	22	5	2	N	Recovered / resolved
			10	M	Blastocystis hominis diarrhea	Blastocystis infection	Infections and infestations	HO	1	23	5	2	N	Recovered / resolved
			10		Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	23	12	2	N	Recovered / resolved

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
MED = Medical Advice

Table 207 Listing of SAEs reported within the 28-day (Days 0-27) post-vaccination period (By age strata - Total Vaccinated cohort)

Group	Sub group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
Q-QIV	6-17M	(b) (6)		16	M	Acute diahrrea	Diarrhoea	Gastrointestinal disorders	HO	2	3	7	2	N	Recovered / resolved
D-TIV-YB	6-17M			13	M	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	22	5	2	N	Recovered / resolved
				10	M	Blastocystis hominis diarrhea	Blastocystis infection	Infections and infestations	HO	1	23	5	2	N	Recovered / resolved
				10		Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	23	12	2	N	Recovered / resolved

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
MED = Medical Advice

Table 208 Listing of SAEs reported within the 28-day (Days 0-27) post-vaccination period (By priming status - Total Vaccinated cohort)

Group	Sub group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
Q-QIV	UNPRIM	(b) (6)		16	M	Acute diahrrea	Diarrhoea	Gastrointestinal disorders	HO	2	3	7	2	N	Recovered / resolved
D-TIV-YB	UNPRIM			13	M	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	22	5	2	N	Recovered / resolved
				10	M	Blastocystis hominis diarrhea	Blastocystis infection	Infections and infestations	HO	1	23	5	2	N	Recovered / resolved
				10		Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	23	12	2	N	Recovered / resolved

Q-QIV = Flu Q-QIV Vaccine
D-TIV-YB = *Fluarix* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
MED = Medical Advice

13.2. CIOMS reports

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Bronchiolitis

This male subject was enrolled in the prophylactic observer double-blind study 116926 (FLU D-QIV-013).
On (b) (6), he received a 1st dose of of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 22 days after the 1st dose of Blinded vaccine, this 14-month-old subject developed bronchiolitis. The subject was hospitalised. The subject was treated with Dextrose in normal saline, ceftriaxone, hydrocortisone, salbutamol sulphate and acetylcysteine. The event resolved on (b) (6). The investigator considered that there was no reasonable possibility that the bronchiolitis may have been caused by investigational product.

The symptoms began on (b) (6) with respiratory distrest that

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Intramuscular

17. INDICATION(S) FOR USE: Unknown

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

14. DENTIF ED DRUG(S)

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023597A

24c. DATE RECEIVED	DATE OF REPORT
28DEC2012	19JUN2013

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ NITIAL ☐ FOLLOW-UP

R0023597A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

worsened the next day is brought on (b) (6) at the emergency and was admitted , respiratory distrest end on 18 dec 2012. Discharge date was on (b) (6) , recovered . Chest X ray showed lung hyperinflation.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Blastocystis infection, Bronchiolitis

This male subject was enrolled in the prophylactic observer double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 23 days after the 1st dose of Blinded vaccine, this 11-month-old subject developed blastocystis hominis diarrhea and bronchiolitis. The subject was hospitalized. The subject was treated with Dextrose in normal saline, saccharomyces boulardii, Pedialyte, ambroxol, hydrocortisone, metronidazole, prednisolone, salbutamol sulphate and aminoside. Blastocystis hominis diarrhea resolved on 31 December 2012. Bronchiolitis resolved on 07 January 2013. The investigator considered that there was no reasonable possibility that the blastocystis hominis diarrhea and bronchiolitis may have been caused by investigational product.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S): Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S):

15. DA LY/CUMULATIVE DOSE:

16. ROUTE OF ADM NISTRATION:

17. INDICATION(S) FOR USE:

18. THERAPY DATES (From / To):

19. THERAPY DURATION:

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023657A

24c. DATE RECEIVED: 26APR2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

R0023657A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Investigator Comments:
male infant who presented liquid stools more than 5 times on 27 dec 2012, started coughing on 27 Dec 2012, was admitted on (b) (6) with a diagnosis of acute diarrhea . Physical examination auscultate
d bilaterales wheezing and rhonchi and was considered as a second diagnosis bronchiolitis.
liquid stools 5 times on 28 dec 2012, 11 times on 29 dec 2012 and 7 times on 30 dec 2012, 3 times on 31 dec 2012, showed improvement in cough and wheeze and was di
scharged on (b) (6) with outpatient drugs such as prednisolone, Perenterol, ambroxol and aminosidine.
Chest x ray Showed bronchial hyperreactivity, CBC, sodium and potassium was normal, stool test Showed hominis blasts
Cough end on 07 jan 2013.

Stool test on (b) (6) showed hominis blasts.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
CHLORIDE	(b) (6)	108.5MEQ/L	98	106
HEMATOCRIT		36.7%	37	50
HEMATOCRIT		36.3%	37	50
HEMOGLOBIN		12.1G/DL	12	17
HEMOGLOBIN		12G/DL	12	17
LYMPHOCYTES		56.5%	28	50
NEUTROPHILS		29.3%	37	72
PLATELET COUNT		560/MM3	150	430
POTASSIUM		5.06MEQ/L	3.5	5.3
SODIUM		141.6MEQ/L	135	145
WHITE BLOOD CELL COUNT		16.6/MM3	4	10
WHITE BLOOD CELL COUNT		8.8/MM3	4	10

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		F	(b) (6)

7. & 13. DESCR BE EVENT(S)

Dehydration

This female subject was enrolled in the prophylactic observer double-blind study 116926 (FLU D-QIV-013).

On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 37 days after the 2nd dose of Blinded vaccine, two days after the last intake of Amoxillin, one days after last intake of Azithromycin, and same day after taking Azithromycin, this 16-month-old subject developed dehydration. The subject was hospitalised. The event resolved on 13 January 2013. The investigator considered that there was no reasonable possibility that the dehydration may have been caused by investigational product, and that the event was possibly due to Amoxillin and

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) 1) Blinded vaccine Injection (Blinded vaccine trial med)
GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Unknown

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S) 2) Amoxicillin trihydrate

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Oral

17. INDICATION(S) FOR USE: ACUTE PHARYNGITIS

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	6 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023722A

24c. DATE RECEIVED: 14JAN2013

DATE OF REPORT: 21JAN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☒ NITIAL ☐ FOLLOW-UP

INTERNATIONAL EVENT REPORT

DESK COPY (Page 2 of 3)

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		F	(b) (6)

7. & 13. DESCR BE EVENT(S)

Azithromycin (unknown manufacturer).

This 15 month old child presented to the ER (b) (6) with diarrehea since jan 9th 2013 after taking amoxicillin/azythromycin. She was having large bowel movements 4 to 5 times a day. stool was watery and yellow with no blood present. she had reduced appetite. she also had reduced urinary output. no significant past medical history no known allergies. immunizations are up to date. physical exam: she looked unwell she had mild dehydration ear nose and throat was significant for rhinnorhea ear drums and throat appeared normal. there was no cervical lymphadenopathy. chest examination demonstrated good air entry bilaterally. there were no added sounds. there was no respiratory distress. cardivascular exam: heart sounds were normal with no murmurs. abdomen was soft with no masses. central nervous system: Alert and anxious child. there was no neck stiffness. she was admitted to hospital for intravenous hydration all other medications were stopped. according to the mother the child slowly recovered and was discharged home (b) (6). There were no medications at discharge.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) 3) Azithromycin

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Oral

17. INDICATION(S) FOR USE: ACUTE PHARYNGITIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S) 4) Azithromycin

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Oral

17. INDICATION(S) FOR USE: ACUTE PHARYNGITIS

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 3 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

R0023722A

24c. DATE RECEIVED: 14JAN2013

DATE OF REPORT: 21JAN2013

24d. REPORT SOURCE ☐ HEALTH PROFESSIONAL ☐ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ NITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
BLOOD GLUCOSE	(b) (6)	5.2MMOL/L	2.5	5.0
CARBON DIOXIDE		19MMOL/L	22	31
CHLORIDE		105MMOL/L	99	111
CREATININE		38MMOL/L	0	36
POTASSIUM		5.3MMOL/L	3.7	5.0
SODIUM		135MMOL/L	135	143
UREA		4.9MMOL/L	1.8	5.4

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Bronchial hyperreactivity, Asthma

This male subject was enrolled in the prophylactic observer double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 33 days after the 2nd dose of Blinded vaccine, this 19-month-old subject developed reactive airway disease and asthma. The subject was hospitalized. The subject was treated with salbutamol sulphate, paracetamol, prednisolone and prednisone. The events resolved on 23 January 2013. The investigator considered that there was no reasonable possibility that the reactive airway disease and asthma may have been caused by investigational product.

Investigator Comment: Subject s parent brought subject in to the Emergency Room (b) (6) because the subject was not breathing

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S)

15. DA LY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023791A

24c. DATE RECEIVED: 26MAR2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

properly. The subject was admitted on (b) (6) . A nasal swab and x-ray were taken. The x-ray showed spots on lung as per f
ather. The subject was given ventolin and prednisolone. On 22jan2013 the prednisolone was changed to prednisone. The subject was released on (b) (6) with a prescription ofor prednisone (taken until 25jan2013) and Apo-Salvent (ongoing PRN). Medical Recor
ds requested 25jan2013.
The diagnosis of the condition was reactive airway disease/asthma. (this information added on 31 Jan 2013).

Nasal swab - respiratory syncytial virus - RSV negative (b) (6)
Nasal swab - influenza and parainfluenza - Results pending (b) (6)
Nasal swab results received (b) (6) . Results for influenza, parainfluenza 1, 2, 3, human metapneumovirus, adnovirus all negative/not detected.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Diarrhoea

This male subject was enrolled in the prophylactic observer double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), three days after the 2nd dose of Blinded vaccine, this 16-month-old subject developed acute diarrhea. The subject was hospitalised. The subject was treated with Dextrose in normal saline, saccharomyces boulardii and Pedialyte. The event resolved on 06 January 2013. The investigator considered that there was no reasonable possibility that the acute diarrhea may have been caused by investigational product.

Investigator Comments:
The subject had liquid stools 4 times a day to start wl (b) (6)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S)

15. DA LY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023792A

24c. DATE RECEIVED: 18MAR2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

and ended on 06 jan 2013, was taken to his doctor on (b) (6) and that same day he was admitted to the clinic. stool tests performed was negative , Discharge date was on (b) (6)

Test on Stool on (b) (6), the result was negative.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		F	(b) (6)

7. & 13. DESCR BE EVENT(S)

Pharyngitis streptococcal

This female subject was enrolled in the prophylactic observer double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 32 days after the 2nd dose of Blinded vaccine, this 20-month-old subject developed streptococcus pharyngitis group A. The subject was hospitalized. The subject was treated with cephalexin and cefuroxime sodium. The event resolved on 15 February 2013. The investigator considered that there was no reasonable possibility that the streptococcus pharyngitis group A may have been caused by investigational product.

Investigator Comments:
Admitted on (b) (6) for possible diagnosis of Kawasaki disease.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S)

15. DA LY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023872A

24c. DATE RECEIVED: 05JUN2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

R0023872A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Subject had Fever since 3 days according to mother and no other symptoms. Awaiting hospital s report.
(b) (6) Discussed with hospital nurse, was discharged from hospital (b) (6) and was seen at follow-up clinic on (b) (6) . Final diagnosis is streptococcus pharyngitis. Was feeling fine yesterday according to hospital nurse. Report from hospital to come.
28feb2013: Hospital report shows Streptococcus A infection of throat and non-deficient microcytic anaemia. Very good evolution with I.V. and then per os antibiotics.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Pneumonia aspiration

This male subject was enrolled in the prophylactic observer double-blind study 116926 (FLU Q-QIV-013).

On (b) (6) he received a 1st and 2nd dose of of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 59 days after the 2nd dose of Blinded vaccine, this 14-month-old subject developed pneumonia by immersion. The subject was hospitalized. The subject was treated with Dextrose in normal saline, ceftriaxone, paracetamol, oxygen, cefadroxil and ambroxol. The event resolved on 25 February 2013. The investigator considered that there was no reasonable possibility that the pneumonia by immersion may have been caused by investigational product.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Intramuscular

17. INDICATION(S) FOR USE: Unknown

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

14. DENTIF ED DRUG(S)

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

18. THERAPY DATES (From / To)	19. THERAPY DURATION

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023932A

24c. DATE RECEIVED	DATE OF REPORT
20MAR2013	19JUN2013

24d. REPORT SOURCE ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE ☐ NITIAL ☐ FOLLOW-UP

R0023932A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Investigator comment: Male infant was admitted at the hospital on (b) (6) by emergency due to being submerged in a cube with water, the infant had dehydration and bilateral ronchis.
Chest x rays showed: Bilateral infiltrate.
Male infant was withdra from the hospital on (b) (6) with outpatient treatment of Cefadroxil + Ambroxol.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Canada	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Bacterial pyelonephritis

This male subject was enrolled in the prophylactic observer double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 57 days after the 2nd dose of Blinded vaccine, this 13-month-old subject developed enterococcus pyelonephritis. The subject was hospitalised. The subject was treated with amoxicillin trihydrate. The event resolved on 25 February 2013. The investigator considered that there was no reasonable possibility that the enterococcus pyelonephritis may have been caused by investigational product.

Investigator Comments:
Subject started fever on (b) (6). Was seen at hospital on (b) (6)

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S): Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S):

15. DA LY/CUMULATIVE DOSE:

16. ROUTE OF ADM NISTRATION:

17. INDICATION(S) FOR USE:

18. THERAPY DATES (From / To):

19. THERAPY DURATION:

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0023956A

24c. DATE RECEIVED: 09APR2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

R0023956A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

(b) (6) with a fever at 41.2 celcius. Subject was hospitalized on (b) (6) and investigated. Subject reportedly had lumbar punction, blood sampling, chest X-ray and kindey-ultrasound. Investigation showed urinary tract infection and vesico-uretral reflux. Subject was treated with Amoxicilline po BID. Discharged on (b) (6) .
28feb2013: Hospital report shows an Acute pyelonephritis due to Enterococcus faecalis, inflammatory anaemia (related to acute infection) and mild splenomegalia for which a control ultra sound is suggested in 3 months, lumbar punction was negative.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
HEMOGLOBIN	(b) (6)	95G/L	105	135

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Dengue fever

This male subject was enrolled in the prophylactic observer double-blind study 116926 (FLU Q-QIV-013).

On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 63 days after the 2nd dose of Blinded vaccine, this 30-month-old subject developed dengue. The subject was hospitalised. The subject was treated with Ringer lactate and paracetamol. The event resolved on 25 February 2013. The investigator considered that there was no reasonable possibility that the dengue may have been caused by investigational product.

Investigator comments: 30 months male infant that was admited to the hospital via emergency on (b) (6) with syntoms of fever that

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S)

15. DA LY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0024035A

24c. DATE RECEIVED: 07MAR2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

R0024035A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

started on (b) (6) 39.0 Celsius, (b) (6) 40.0 Celsius, (b) (6) 38.0 Celsius, (b) (6) 37.1 Celsius, (b) (6) 38.
5 Celsius, (b) (6) 39.0 Celsius, (b) (6) 37.3 Celsius. The symptoms finished on 25Feb2013. The discharge date was on (b) (6)

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
PLATELET COUNT	(b) (6)	133000/MM3	150000	450000
PLATELET COUNT		113000/MM3	150000	450000
PLATELET COUNT		96000/MM3	150000	450000
PLATELET COUNT		280000/MM3	150000	450000

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		F	(b) (6)

7. & 13. DESCR BE EVENT(S)

Gastroenteritis rotavirus

This female subject was enrolled in the prophylactic double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 92 days after the 2nd dose of Blinded vaccine, this 24-month-old subject developed rotavirus gastroenteritis. The subject was hospitalised. The subject was treated with Lactated ringer's solution, Dextrose + normal saline, bacillus subtilis spores, Pedialyte and paracetamol. The event resolved on 26 March 2013. The investigator considered that there was no reasonable possibility that the rotavirus gastroenteritis may have been caused by investigational product.

Investigator Comments:

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S)

15. DA LY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0024158A

24c. DATE RECEIVED: 13MAY2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

2 years old female infant who started on (b) (6) with liquid stools 5-6 times until 26 Mar 2013 and began vomiting on 21 Mar 2013 until 25 Mar 2013 and 21 Mar 2013 fever 38.5 to 24 Mar 2013.
On (b) (6) she was taken to the emergency room where she was treated with 500 cc intravenous lactate solution , stool test performed was negative and was sent home with oral hydration,and acetaminophen, symptoms worsened and was taken again on (b) (6) and was admitted (b) (6), stool test performed Showed rotavirus, discharge date was on (b) (6).

Stool test showed rotavirus

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		F	(b) (6)

7. & 13. DESCR BE EVENT(S)

Rotavirus infection

This female subject was enrolled in the prophylactic double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), she received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 81 days after the 2nd dose of Blinded vaccine, [drug time to onset since last dose] after the [dose number] dose of No therapy, this 18-month-old subject developed rotavirus infection. The subject was hospitalised. The subject was treated with metronidazole, Dextrose in normal saline, dimenhydrinate, ranitidine hydrochloride and saccharomyces boulardii. The event resolved on 11 April 2013. The investigator considered that there was no reasonable possibility that the rotavirus infection may have been caused by investigational product and No therapy and that the event was possibly due to [other contributing factors].

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S)	15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION	17. INDICATION(S) FOR USE	18. THERAPY DATES (From / To)	19. THERAPY DURATION	20. DID EVENT ABATE AFTER STOPP NG DRUG?	21. DID EVENT REAPPEAR AFTER REINTRODUCTION?
Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline	Unknown	Intramuscular	PROPHYLAXIS	(b) (6)	1 Days	☐ YES ☐ NO ☒ N/A	☐ YES ☐ NO ☒ N/A
No therapy	Unknown	Unknown	Unknown	Unknown	Unknown	☐ YES ☐ NO ☒ N/A	☐ YES ☐ NO ☒ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0024209A

24c. DATE RECEIVED: 17JUN2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE

☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE

☐ NITIAL ☐ FOLLOW-UP

R0024209A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

Investigator Comments : Female infant was admitted to the hospital on (b) (6) due to persistent diarrhea which started on (b) (6). The subject still not recovered from this episode.
Stool culture on (b) (6) result positive
for Rotavirus, the subject was discharged from the hospital on (b) (6) with outpatient treatment of Parenterol which started on (b) (6) and finished 12APR2013.
Symptoms ended on 11APR2013, Subject is recovered/resolved.

Stool culture on (b) (6) result: positive for Rotavirus

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
HEMATOCRIT	(b) (6)	37%	37.0	50.0
LYMPHOCYTES		56%	28	50
NEUTROPHILS		32.8%	37	72
PLATELET COUNT		410/MM3	150	450
POTASSIUM		4.37MEQ/L	3.5	5.3
RED BLOOD CELL COUNT		4.95/MM3	3.50	5.30
SODIUM		140.9MEQ/L	135	145
WHITE BLOOD CELL COUNT		7.3/MM3	4	10

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Amoebic dysentery

This male subject was enrolled in the prophylactic double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 89 days after the 2nd dose of Blinded vaccine, this 11-month-old subject developed intestinal amebiasis. The subject was hospitalised. The subject was treated with Normosol and metronidazole. The event resolved on 14 April 2013. The investigator considered that there was no reasonable possibility that the intestinal amebiasis may have been caused by investigational product.

Investigator Comments :
Male infant was admitted to the hospital on (b) (6), due to

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION
Unknown	Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To)	19. THERAPY DURATION
(b) (6)	1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S)

15. DA LY/CUMULATIVE DOSE	16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)	19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0024214A

24c. DATE RECEIVED: 13MAY2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

presenting diarrheal stools on (b) (6) .Stool test on (b) (6) results negative.The subject was dispatched from the hospital on (b) (6) , without outpatient drugs, still recovering from diarrhea.The subject was admitted again to the hospital on (b) (6) due to presenting diarrheal stools 16 times on (b) (6) .Stool test on (b) (6) result positive for Amebiasis. Subject was dispatched from the hospital on (b) (6) , with Flagenose as outpatient drug, the symptoms finished on 14APR2013. Episode resolved subject recovered.

Stool test on (b) (6) , result: Negative.Stool test on (b) (6) , result: Positive for Amebiasis.

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

Protocol No: 116926

Eudract No:

Subj. ID: (b) (6) Treat. No:

I. EVENT INFORMATION

1. PAT ENT NITIALS	1a. COUNTRY	2. DATE OF B RTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
(b) (6)	Dominican Republic	(b) (6)		M	(b) (6)

7. & 13. DESCR BE EVENT(S)

Gastroenteritis rotavirus

This male subject was enrolled in the prophylactic double-blind study 116926 (FLU Q-QIV-013).
On (b) (6), he received a 1st and 2nd dose of Quebec quadrivalent influenza vaccine (Flu Q-QIV 15mcg HA/strain) or trivalent influenza vaccine (Fluarix YB identical to Fluarix with Yamagata lineage B strain).

On (b) (6), 83 days after the 2nd dose of Blinded vaccine, this 17-month-old subject developed rotavirus gastroenteritis. The subject was hospitalised. The subject was treated with Dextrose in normal saline, paromomycin, bacillus subtilis spores. The event resolved on 05 April 2013. The investigator considered that there was no reasonable possibility that the rotavirus gastroenteritis may have been caused by investigational product.

Investigator Comments :
Male infant was admitted to the hospital on (b) (6) due to

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT D ED AS OUTCOME OF EVENT
- ☒ RESULTED IN OR PROLONGED INPAT ENT HOSPITALISATION
- ☐ NVOLVED PERSISTENCE OF SIGNIFICANT DISAB LITY OR INCAPACITY
- ☐ LIFE THREATEN NG
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. DENTIF ED DRUG(S) Blinded vaccine Injection (Blinded vaccine trial med) GlaxoSmithKline

15. DA LY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADM NISTRATION: Intramuscular

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): (b) (6)

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. DENTIF ED DRUG(S)

15. DA LY/CUMULATIVE DOSE

16. ROUTE OF ADM NISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPP NG DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Global Clinical Safety
1250 South Collegeville Rd.,
Collegeville, PA, 19426-0989, US

R0024215A

24c. DATE RECEIVED: 13MAY2013

DATE OF REPORT: 19JUN2013

24d. REPORT SOURCE: ☒ HEALTH PROFESSIONAL ☒ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ NITIAL ☐ FOLLOW-UP

R0024215A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

presenting diarrhea and vomiting on (b) (6) . Diarrhea finished on 05APR2013, and vomiting finished on 02APR2013. Stool test negative, cultive on stool result positive for Rotavirus, the subject was dispatched from the hospital on (b) (6) .Recovered.

Stool test on (b) (6) , result: negative.Cultive on Stool on (b) (6) , result: positive for Rotavirus.

GlaxoSmithKline Biologicals, SA

Study detailed title

A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine *Fluzone*®, administered intramuscularly to children 6 to 35 months of age.

Clinical Study Report for Study 200806 (FLU Q-QIV-021)

This report provides immunogenicity and safety results obtained from Day 0 to Day 180.

Development Phase II

IND Number: BB-IND 14466

Name of Investigational Product: GlaxoSmithKline (GSK) Biologicals' quadrivalent (QIV) influenza vaccine (GSK2282512A)

Indication Studied: Immunization against influenza in male and female subjects 6 to 35 months of age inclusive.

Study initiation date:	23-October-2013
Study completion date:	03-July-2014
Data lock point (Date of database freeze):	30-October-2014
Date of report:	Final: 12 December 2014

Sponsor Signatory: Varsha K. Jain, MD
Director, Clinical Development Flu Vaccine
GlaxoSmithKline Biologicals

This study was performed according to the principles of GCP including the archiving of essential documents.

Based on GSK Biologicals' Study Report INS-BIO-CLIN-1010 v05

SYNOPSIS

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

Study No.: 200806 (FLU Q-QIV-021)

Title of the study: A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Bio10logicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine *Fluzone*®, administered intramuscularly to children 6 to 35 months of age.

Investigator(s) and study centre(s):
Multicenter study in United States of America (USA).
Principal investigator: Joseph Domachowske, Department of Pediatrics, SUNY Upstate Medical Center, Syracuse, NY, USA

Publication (reference):
None at the time of this report.

Study period: **Study initiation date:** 23-October-2013 **Study completion date:** 03-July-2014 **Data lock point (Date of database freeze):** 30-October-2014	**Phase:** II

Indication: Immunization against influenza in male and female subjects 6 to 35 months of age inclusive.

Objectives:

Primary

- To assess the immunogenicity of FLU Q-QIV based on CBER's seroconversion rate (SCR) criterion for each of the four strains in children 6 to 35 months of age, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).
  Criterion for determination of effective immunization:
  - The lower limit (LL) of the two-sided 95% confidence interval (CI) for SCR should be ≥ 40% for each strain.

Secondary

- To test the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of GMT and SCR) in all subjects approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively) by comparing FLU Q-QIV to *Fluzone*.
  Criteria to conclude superiority of the B/Victoria strain:
  Immunogenic superiority of the B/Victoria strain would be concluded if
  - The LL of the two-sided 95% CI of the geometric mean titre (GMT) ratio (FLU Q-QIV/*Fluzone*) was greater than 1.5, and
  - The LL of the two-sided 95% CI for the SCR difference (FLU Q-QIV minus *Fluzone*) was greater than 10%.
- To describe the immunogenicity (in terms of GMTs, seroprotection rates [SPRs], SCRs and mean geometric increases [MGIs]) of FLU Q-QIV and *Fluzone*.
- To describe the reactogenicity and safety of FLU Q-QIV and *Fluzone* in terms of:
  - Solicited local and general AEs during the 7-day post-vaccination follow-up period (day of vaccination and six subsequent days).
  - Unsolicited AEs during the 28-day post-vaccination follow-up period (day of vaccination and 27 subsequent days).

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

- Serious adverse events (SAEs), medically attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period.
- To evaluate the relative risk of fever of FLU Q-QIV compared to *Fluzone* during a 4-day follow-up period.

Tertiary

- To describe the GMT ratio and SCR difference of FLU Q-QIV vs *Fluzone* for the three common strains present in both vaccines:
  - GMT ratio (*Fluzone*/Q-QIV) with 95% CI

SCR difference (*Fluzone minus Q-QIV*) with 95% CI.

Methodology: This is a phase II, observer blind, randomised (1:1), controlled, multicentre study with two parallel groups (Q-QIV and TIV-YB groups). The subjects received vaccination as per their priming status. Subjects in the Q-QIV group received the Flu-Q-QIV vaccine and subjects in the TIV-YB group received the *Fluzone* vaccine (one dose on Day 0 if primed, two doses, on Day 0 and Day 28, if unprimed). Blood samples were collected on Days 0 and 28 for primed subjects and on Days 0 and 56 for unprimed subjects.

Study vaccine, dose, mode of administration, lot no.:

Vaccination schedule /site:

One or two intramuscular (IM) injection(s) in the anterolateral side of left thigh (subjects < 12 months of age) or in the deltoid muscle of the non-dominant arm (subjects ≥ 12 months of age) on Day 0 (primed subjects) or Day 0 and Day 28 (unprimed subjects).

Vaccine composition /dose /lot number:

The quadrivalent influenza virus (FLU Q-QIV) candidate vaccine contained haemagglutinin (HA) from four influenza strains with a total of 60 µg (15 µg for each strain): A/California/7/2009 (H1N1 pdm09), A/Texas/50/2012 (H3N2), and B/Massachusetts/2/2012 (Yamagata lineage) and B/Brisbane/60/2008 (Victoria lineage). The total volume injected was 0.5 mL. The lot number was DFLHA804A.

Reference vaccine /Comparator, dose and mode of administration, lot no.:

Vaccination schedule /site:

One or two IM injection(s) in the anterolateral side of left thigh (subjects < 12 months of age) or in the deltoid muscle of the non-dominant arm (subjects ≥ 12 months of age) on Day 0 (primed subjects) or Day 0 and Day 28 (unprimed subjects).

Vaccine composition /dose /lot number:

The trivalent control vaccine (TIV-YB), commercially available as *Fluzone,* contained HA from three influenza strains with a total of 22.5 µg (7.5µg for each strain): A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), and B/Massachusetts/2/2012 (Yamagata lineage). The total volume injected was 0.25 mL. The lot numbers were DLOCA085A (U4694EA), DLOCA097A (U4694EA), DLOCA100A (U4711DA).

Study Population:

The study enrolled eligible subjects with stable health between the age of 6 and 35 months, and for whom the investigator determined that their parents/LARs could and would comply with the requirements of the protocol. Written informed consent was obtained from the parent(s)/LAR(s) of the subject. Study criteria leading to the exclusion of a subject from the study included administration of an influenza vaccine or chronic use of immune-modifying drugs within 6 months prior to the first vaccine dose, any investigational or non-registered drug within 30 days prior to or during the study;

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

immunoglobulins and/or any blood products within the three months before study entry; confirmed or suspected immunosuppressive or immunodeficient condition, history of Guillain-Barré syndrome within 6 weeks of receipt of prior inactivated influenza virus vaccine, any known or suspected allergy to any constituent of influenza vaccines, any significant disorder of coagulation or treatment with warfarin derivatives or heparin and any other condition which, in the opinion of the investigator, which would have prevented the subject from participating in the study.

Duration of treatment:
The duration of the study was approximately six months for each subject.

Criteria for evaluations:

Primary endpoint(s):

- Humoral immune response to each strain of FLU Q-QIV. Serum HI antibodies on Day 0 and 28 days after the last vaccine dose were used to calculate:
  - SCRs

Secondary endpoints:

- Humoral immune response against the B/Victoria strain. Serum HI antibody titres for the B/Victoria strain 28 days after the last vaccine were used to calculate:
  - GMT ratio (Q-QIV/*Fluzone*)
  - SCR difference (Q-QIV minus *Fluzone*)
- Humoral immune response to each strain. Serum HI antibody titres on Day 0 and 28 days after the last vaccine from both vaccine groups were used to calculate:
  - GMTs
  - SCRs
  - SPRs
  - MGIs
- Solicited local and general AEs
  - Occurrence of solicited local and general AEs (summarised by incidence rate, duration, intensity and relationship to vaccination [general AEs]) during a 7-day follow-up period (i.e., day of vaccination and six subsequent days) after each vaccination, in each group.
- Unsolicited AEs
  - Occurrence of unsolicited AEs (summarised by incidence rate, intensity, and relationship to vaccination) during a 28-day follow-up period (i.e., day of vaccination and 27 subsequent days) after each vaccination, in each group.
- MAEs, SAEs, and pIMDs
  - Occurrence of MAEs, SAEs and pIMDs (summarised by incidence rate and relationship to vaccination) during the entire study period.
- Occurrence of any fever (≥ 38°C) or grade 3 fever or higher (> 39°C) during a 4-day follow-up period after Dose 1 or Dose 2

Tertiary endpoints

- Humoral immune response against the three common strains. Serum HI antibody titres 28 days after the last vaccine were used to calculate (for the three common strains):
  - GMT ratio (*Fluzone*/Q-QIV)
  - SCR difference (*Fluzone* minus Q-QIV)

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

Statistical methods:

Analysis of demographics and other baseline characteristics: Demographic characteristics (age, height, weight, gender and race) of each study vaccine group were tabulated for all subjects, by age stratum and priming status. Summary statistics for subjects' age, classified by gender of the vaccinated subjects as a whole and per study group, were calculated.

Analysis of immunogenicity: The primary analysis was based on the according to protocol (ATP) cohort for analysis of immunogenicity. As the percentage of vaccinated subjects excluded from the ATP cohort for analysis of immunogenicity was more than 5%, a second analysis based on the total vaccinated cohort (TVC) was performed to complement the ATP analysis.

Within groups assessment: To assess the primary objective, SCR 28 days following last vaccination was calculated. The primary objective would be met if the LL of the two-sided 95%CI for SCR was ≥ 40% for each strain in Flu Q-QIV. MGI, 28 days following last vaccination, GMT of HI, and SPR at Day 0 and 28 days following last vaccination, were calculated by group for all subjects, each age strata (6 to 17 and 18 to 35 months of age) and by priming status (primed and unprimed) with 95% CI.

Between groups assessment: To assess the immunogenic superiority of the B/Victoria strain, the GMT ratio of FLU Q-QIV over *Fluzone* and the two-sided 95% CI and the SCR difference (FLU Q-QIV minus *Fluzone*) and the 95% CI were calculated. The superiority of FLU Q-QIV over *Fluzone* would be concluded if the LL of two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluzone*) was > 1.5 and the LL of two-sided 95% CI on the SCR difference (FLU Q-QIV minus *Fluzone*) was > 10%.

To assess the immunogenic difference between FLU Q-QIV and *Fluzone* for the three common strains (H1N1, H3N2 and B/Yamagata),, the GMT ratio of *Fluzone* over FLU Q-QIV (*Fluzone*/FLU Q-QIV) and the two sided 95% CI and the difference of SCR (*Fluzone* – FLU Q-QIV) and the two-sided 95% CI were calculated.

Analysis of safety: The primary analysis was performed on the TVC. As the percentage of subjects excluded from the ATP cohort for analysis of safety was lesser than 5%, a secondary analysis was not performed on this ATP cohort.

Within groups assessment:

- The percentage of subjects with at least one local AE (solicited only), with at least one general AE (solicited only) and with any AE during the 7-day follow-up period was tabulated with exact 95% CI after each vaccine dose and overall. The percentage of doses followed by at least one local AE (solicited only), by at least one general AE (solicited only) and by any AE during the defined follow-up period was tabulated with exact 95% CI. The same calculations were performed for AEs rated as grade 3, related AEs and grade 3 related AEs.
- The percentage of subjects reporting each individual solicited local (any, grade 3, and medically attended) and general (any, grade 3, related, grade 3 related and medically attended) AE during the 7-day solicited follow-up period was tabulated with exact 95% CI. The percentage of doses followed by each individual solicited local and general AE during the 7-day solicited follow-up period was tabulated with exact 95% CI.
- The percentage of subjects with at least one report of unsolicited AE classified by MedDRA PT and reported up to 27 days after vaccination was tabulated with exact 95% CI. The same tabulations were performed for grade 3 unsolicited AEs, for unsolicited AEs with a causal relationship to vaccination and grade 3 unsolicited AEs with a causal relationship to vaccination.
- MAEs, SAEs and pIMDs were collected and summarised through the entire follow up period (180 days). In addition, SAEs and withdrawal due to AEs were to be described in detail.

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

Table 1: Study population (Total Vaccinated cohort):

Number of subjects	**Q-QIV**	**TIV-YB**	**Total**
Planned, N	250	250	500
Randomised, N (Total Vaccinated Cohort)	158	156	314
Completed Month 6 visit, n (%)	143 (90.5)	141 (90.4)	284 (90.4)
Demographics	**Q-QIV**	**TIV-YB**	**Total**
N (Total Vaccinated Cohort)	158	156	314
Females:Males	74:84	82:74	156:158
Mean Age, months (SD)	19.6 (8.8)	19.8 (8.9)	19.7 (8.9)
Median Age, months (minimum, maximum)	21 (6, 35)	21 (6, 35)	21 (6, 35)
White - Caucasian / European Heritage, n (%)	86 (54.4)	88 (56.4)	174 (55.4)
African Heritage / African American, n (%)	56 (35.4)	56 (35.9)	112 (35.7)
Others, n (%)	13 (8.2)	11 (7.1)	24 (7.6)

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N=total number of subjects
n/%=number/percentage of subjects
SD=standard deviationa

Summary:

Immunogenicity results:

- The primary immunogenicity objective was met, as the LL of the two-sided 95% CI for SCR was > 40% against all four strains (range 58.1% to 79.2%), approximately 28 days after completion of dosing.
- The confirmatory secondary objective was also met. The immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of adjusted GMT ratios and SCR difference) was concluded, as the LL of the two-sided 95% CI of the adjusted GMT ratio (FLU Q-QIV/Fluzone), 3.73, was greater than 1.5, and the LL of the two-sided 95% CI for the SCR difference (FLU Q-QIV minus Fluzone), 43.88%, was greater than 10%.

Table 2: Seroconversion rate (SCR) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for FLU Q-QIV and FLU TIV-YB (ATP cohort for immunogenicity)

			SCR			
					95% CI	
Antibody	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	143	115	80.4	73.0	86.6
	TIV-YB	137	98	71.5	63.2	78.9
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	143	103	72.0	63.9	79.2
	TIV-YB	137	94	68.6	60.1	76.3
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	143	123	86.0	79.2	91.2
	TIV-YB	137	115	83.9	76.7	89.7
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	143	95	66.4	58.1	74.1
	TIV-YB	137	17	12.4	7.4	19.1

Footnotes overleaf

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as :
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects : antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 3: Adjusted GMT ratios of B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: Q-QIV/TIV-YB (ATP cohort for immunogenicity

				Adjusted GMT ratio (Q-QIV / TIV-YB)		
Q-QIV		**TIV-YB**			**95% CI**	
N	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
143	64.7	137	13.7	4.73	3.73	5.99

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Analysis of co-variance (Ancova) model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 4: SCR Difference between groups for B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: Q-QIV minus TIV-YB (ATP cohort for immunogenicity)

							Difference in SCR (Q-QIV minus TIV-YB)		
	Q-QIV			**TIV-YB**				**95% CI**	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	143	95	66.4	137	17	12.4	54.02	43.88	62.87

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as:
For initially seronegative subjects: post-vaccination antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects : antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

Table 5: Seropositivity rates, seroprotection rates (SPR) and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose (ATP cohort for immunogenicity)

				≥ 10 1/DIL				≥ 40 1/DIL				GMT				
						95% CI				95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu A/California/7/2009 H1N1 HI	Q-QIV	PRE	143	56	39.2	31.1	47.7	25	17.5	11.6	24.7	10.3	8.6	12.3	<10.0	226.0
		POST	143	137	95.8	91.1	98.4	125	87.4	80.8	92.4	141.3	115.1	173.5	<10.0	1280.0
	TIV-YB	PRE	137	51	37.2	29.1	45.9	22	16.1	10.3	23.3	10.0	8.3	11.9	<10.0	226.0
		POST	137	130	94.9	89.8	97.9	111	81.0	73.4	87.2	90.8	73.2	112.6	<10.0	1280.0
Flu A/Texas/50/2012 H3N2 HI	Q-QIV	PRE	143	61	42.7	34.4	51.2	29	20.3	14.0	27.8	11.1	9.1	13.5	<10.0	453.0
		POST	143	141	98.6	95.0	99.8	118	82.5	75.3	88.4	100.6	82.6	122.6	<10.0	1280.0
	TIV-YB	PRE	137	58	42.3	33.9	51.1	25	18.2	12.2	25.7	11.5	9.3	14.2	<10.0	453.0
		POST	137	135	98.5	94.8	99.8	110	80.3	72.6	86.6	86.2	70.6	105.4	<10.0	1810.0
Flu B/Massachusetts/2/2012 Yamagata HI	Q-QIV	PRE	143	87	60.8	52.3	68.9	31	21.7	15.2	29.3	14.5	12.1	17.5	<10.0	320.0
		POST	143	142	99.3	96.2	100	135	94.4	89.3	97.6	212.0	174.6	257.3	<10.0	1810.0
	TIV-YB	PRE	137	75	54.7	46.0	63.3	22	16.1	10.3	23.3	12.3	10.3	14.7	<10.0	453.0
		POST	137	133	97.1	92.7	99.2	124	90.5	84.3	94.9	140.0	113.9	172.0	<10.0	2560.0
Flu B/Brisbane/60/2008 Victoria HI	Q-QIV	PRE	143	35	24.5	17.7	32.4	13	9.1	4.9	15.0	7.7	6.6	9.1	<10.0	640.0
		POST	143	135	94.4	89.3	97.6	101	70.6	62.4	77.9	69.0	54.9	86.6	<10.0	3620.0
	TIV-YB	PRE	137	25	18.2	12.2	25.7	9	6.6	3.0	12.1	6.6	5.9	7.5	<10.0	226.0
		POST	137	76	55.5	46.7	64.0	27	19.7	13.4	27.4	12.8	10.6	15.4	<10.0	640.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
seropositivity=HI antibody titre ≥ 10 1/DIL
seroprotection=HI antibody titre ≥ 40 1/DIL
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

Table 6: Mean geometric increase (MGI) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose (ATP cohort for immunogenicity)

							MGI ratio			
									95% CI	
Antibody	**Group**	**N**	**Time point description**	**MGI**	**Time point description**	**MGI**	**Ratio order**	**Value**	**LL**	**UL**
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	143	POST	141.3	PRE	10.3	POST / PRE	13.73	11.10	16.99
	TIV-YB	137	POST	90.8	PRE	10.0	POST / PRE	9.11	7.32	11.33
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	143	POST	100.6	PRE	11.1	POST / PRE	9.09	7.69	10.76
	TIV-YB	137	POST	86.2	PRE	11.5	POST / PRE	7.53	6.36	8.90
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	143	POST	212.0	PRE	14.5	POST / PRE	14.59	11.72	18.16
	TIV-YB	137	POST	140.0	PRE	12.3	POST / PRE	11.36	9.09	14.19
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	143	POST	69.0	PRE	7.7	POST / PRE	8.94	7.34	10.89
	TIV-YB	137	POST	12.8	PRE	6.6	POST / PRE	1.93	1.69	2.19

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
MGI = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Safety results:

- *Solicited local AEs*: Overall, injection site pain was the most frequently reported solicited local AE (31.8% and 32.4% of subjects in the Q-QIV and TIV-YB groups, respectively). Grade 3 injection site pain was reported for 2.6% and 0.7% of subjects, respectively.
- *Solicited general AEs*: Overall, irritability/fussiness was the most frequently reported solicited general AE (50.3% and 45.3% of subjects in the Q-QIV and TIV-YB groups, respectively). Grade 3 irritability/fussiness was reported for 8.6% and 4.1% of subjects, respectively. Fever (≥38°C) was reported for 6.6% and 6.8% of subjects in the Q-QIV and TIV-YB groups, respectively. Grade 3 or higher fever (>39.0°C) was reported for 1.3% and 2.0% of subjects, respectively.

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

- *Relative risk of fever:* The relative risk of any fever (≥38°C) for Q-QIV compared to TIV-YB during a 4-day follow-up period was 0.86 with a 95% CI of [0.33; 2.23] (p-value = 0.7969). The relative risk of grade 3 or above fever (>39.0°C) for Q-QIV compared to TIV-YB during a 4-day follow-up period was 0.00 (grade 3 fever was reported for none of the subjects in the Q-QIV group, and for one subject in the TIV-YB group post-dose 1) with a 95% CI of [0.00; 3.76] (p-value = 0.4950).
- *Unsolicited AEs*: During the 28-day post-vaccination period, at least one unsolicited AE was reported for 48.7% and 48.1% of subjects in the Q-QIV and TIV-YB groups, respectively. Diarrhoea (9.5% of subjects) was the most frequently reported AE in the Q-QIV group while in the TIV-YB group, cough (8.3% of subjects) was the most frequently reported AE. At least one grade 3 unsolicited AE was reported for 7.6% and 7.7% subjects in the Q-QIV and TIV-YB groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 7.0% and 4.5 % of subjects, respectively. At least one grade 3 unsolicited AE with causal relationship to vaccination was reported for 2 (1.3%) and 1 (0.6%) of subject(s), respectively.
- *MAEs*: At least one unsolicited AE with a medically attended visit during the entire study period was reported for 48.7% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively. Otitis media was the most frequently reported MAE in both groups (14.6% and 19.2% of subjects, respectively).
- *pIMDs: No* pIMDs were reported in the study.
- *SAEs*: A total of 9 non-fatal SAEs were reported for 9 subjects [5 (3.2%) subjects in the Q-QIV group and 4 (2.6%) subjects in the TIV-YB group] during the entire study period. All events except 2 (sleep apnoea syndrome and convulsion) were considered recovered or resolved at the time of this report. None of these events was considered related to the study vaccine in the opinion of the investigator. No fatal SAEs were reported.
- *Concomitant medication*: Any concomitant medications were used by 51.3% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively, during the entire study period.

Conclusion:

- The primary immunogenicity objective was met, since the LL of the two-sided 95% CI for SCR was >40% against all four strains (range 58.1% to 79.2%), approximately 28 days after completion of dosing.
- The confirmatory secondary objective of demonstrating the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of adjusted GMT ratios and SCR difference) was also met, since the LL of the two-sided 95% CI of the adjusted GMT ratio (FLU Q-QIV/*Fluzone*), 3.73, was greater than 1.5, and the LL of the two-sided 95% CI for the SCR difference (FLU Q-QIV minus *Fluzone*), 43.88% was greater than 10%.
- During the 28-day post-vaccination period, at least one unsolicited AE was reported for 48.7% and 48.1% of subjects in the Q-QIV and TIV-YB groups, respectively. At least one grade 3 unsolicited AE was reported for 7.6% and 7.7% subjects in the Q-QIV and TIV-YB groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 7.0% and 4.5 % of subjects, respectively.
- At least one unsolicited AE with a medically attended visit during the entire study period was reported for 48.7% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively. Otitis media was the most frequently reported MAE in both groups (14.6% and 19.2% of subjects, respectively).

Name of company: **GlaxoSmithKline Biologicals, Rixensart, Belgium**	**Name of finished product:** GSK Biologicals' inactivated quadrivalent influenza vaccine (FLU Q-QIV) – Quebec manufactured	**Name of active substance: [antigen(s)]** A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Brisbane/60/2008 (Victoria lineage) and B/Massachusetts/2/2012 (Yamagata lineage)

- A total of 9 non-fatal SAEs were reported for 9 subjects [5 (3.2%) subjects in the Q-QIV group and 4 (2.6%) subjects in the TIV-YB group] during the entire study period. All events except 2 (sleep apnoea syndrome and convulsion) were considered recovered or resolved at the time of this report. None of these events was considered related to the study vaccine in the opinion of the investigator. No fatal SAEs were reported.
- No other safety concerns were identified. The FLU Q-QIV and *Fluzone* vaccines were generally well tolerated.

Date of report: 12 December 2014

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LIST OF ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
AE	Adverse event
ANCOVA	Analysis of Covariance
ATP	According-to-protocol
CBER	Center for Biologics Evaluation and Research
CHMP	Committee for Medicinal Products for Human Use
CI	Confidence interval
CRDL	Clinical Research and Development Lead
CRO	Contract Research Organisation
CSR	Clinical Study Report
eCRF	Electronic Case Report Form
EMEA	European Medicines Agency
GCP	Good clinical practice
GMT	Geometric mean titre
GSK	GlaxoSmithKline
HI	Haemagglutinin inhibition
IB	Investigators Brochure
IEC	Independent Ethics Committee
IM	Intramuscular
IND	Investigational New Drug
IRB	Institutional Review Board
LAR	Legally Acceptable Representative
LL	Lower Limit
MAE	Medically Attended Adverse Event

MedDRA	Medical Dictionary for Regulatory Activities
MGI	Mean Geometric Increase
pIMD	Potential Immune-Mediated Disease
QIV	Quadrivalent Influenza Vaccine
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SCR	Seroconversion
SOP	Standard Operating Procedures
SPR	Seroprotection
TIV	Trivalent Influenza Vaccine
TVC	Total Vaccinated cohort
WHO	World Health Organization
USA/ US	United States of America

GLOSSARY OF TERMS

Adverse event (AE): Any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e., lack of efficacy), abuse or misuse.

Blinding: A procedure in which one or more parties to the trial are kept unaware of the treatment assignment in order to reduce the risk of biased study outcomes. The level of blinding is maintained throughout the conduct of the trial, and only when the data are cleaned to an acceptable level of quality will appropriate personnel be unblinded or when required in case of a serious adverse event (SAE). In an observer-blind study, the subject and the site and sponsor personnel involved in the clinical evaluation of the subjects are blinded while other study personnel may be aware of the treatment assignment (see Section 5.5 for details on observer-blinded studies).

Child in care: A child who has been placed under the control or protection of an agency, organisation, institution or entity by the courts, the government or a government body, acting in accordance with powers conferred on them by law or regulation. The definition of a child in care can include a child cared for by foster parents or living in a care home or institution, provided that the arrangement falls within the definition above. The definition of a child in care does not include a child who is adopted or has an appointed legal guardian.

Eligible: Qualified for enrolment into the study based upon strict adherence to inclusion/exclusion criteria.

Epoch:	An epoch is a self-contained set of consecutive time points or a single time point from a single protocol. Self-contained means that data collected for all subjects at all time points within that epoch allows to draw a complete conclusion to define or precise the targeted label of the product. Typical examples of epochs are primary vaccinations, boosters, yearly immunogenicity follow-ups, and surveillance periods for efficacy or safety.
eTrack:	GlaxoSmithKline (GSK)'s tracking tool for clinical trials.
Evaluable:	Meeting all eligibility criteria, complying with the procedures defined in the protocol, and, therefore, included in the according-to-protocol (ATP) analysis.
Geometric Mean Titre (GMT):	The anti-log of the mean of the log (base 10) transformed inverse titres (the number X would denote the inverse of a titre expressed as "1:X"). Antibody titres below the cut-off of the assay are given an arbitrary value of half the cut-off for the purpose of GMT calculation.
Immunological correlate of protection:	The defined humoral antibody response above which there is a high likelihood of protection in the absence of any host factors that might increase susceptibility to the infectious agent.
Investigational vaccine/product: **(Synonym of Investigational Medicinal Product)**	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Mean Geometric Increase (MGI):	MGI is defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal haemagglutination inhibition (HI) titre to the pre-vaccination (Day 0) reciprocal HI titre.
Potential Immune-Mediated Disease:	Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.
Prophylactic medication:	Medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination. E.g. an anti-pyretic is considered to be prophylactic when it is given in the absence of fever and any other symptom, to prevent fever from occurring (fever is defined as

	temperature ≥ 38.0°C/100.4°F by any method).
Primed subjects:	All subjects (6 to 35 months of age) who have received a total of two or more doses of seasonal influenza vaccine since 01 July 2010. These subjects will receive only one dose of seasonal influenza vaccine in this study.
Randomisation:	Process of random attribution of treatment to subjects in order to reduce bias of selection.
Self-contained study:	Study with objectives not linked to the data of another study.
Serious Adverse Event (SAE):	Any untoward medical occurrence in a patient or clinical investigation subject that: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.
Seroconversion Rate (SCR):	SCR is defined as the proportion of vaccinees who have either a pre-vaccination titre < 1:10 and a post-vaccination titre ≥ 1:40 or a pre-vaccination titre ≥ 1:10 and at least a four-fold increase in post-vaccination titre.
Seroprotection Rate (SPR):	The seroprotection rate or SPR is defined as the proportion of vaccinees with a serum HI titre ≥ 1:40.
Solicited AE:	AEs to be recorded as endpoints in the clinical study. The presence/occurrence/intensity of these events is actively solicited from the subject or an observer during a specified post-vaccination follow-up period.
Sub-cohort:	A group of subjects for whom specific study procedures are planned as compared to other subjects.
Subject:	Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the clinical study, either as a recipient of the vaccine(s)/product(s) or as a control.
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the study.
Treatment:	Term used throughout the clinical study to denote a set of investigational product(s) or marketed product(s) or placebo intended to be administered to a subject, identified by a unique number, according to the study randomisation or treatment allocation.

Treatment number: A number identifying a treatment to a subject, according to the study randomisation or treatment allocation.

Unprimed subjects: All subjects (6 to 35 months of age) who have never received any seasonal influenza vaccine or have received only one dose of seasonal influenza vaccine since 01 July 2010. These subjects will receive two doses (28 days apart) of seasonal influenza vaccine in this study.

Unsolicited AE: Any AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited AE.

TRADEMARKS

The following trademarks are used in the present report.

Note: In the body of the Study Report, the names of the vaccines/products and/or medications will be written without the superscript symbol ™ or ® and in *italics*.

Trademarks of the GlaxoSmithKline group of companies	Generic description
FluLaval™ Quadrivalent	Inactivated Quadrivalent Split Virion Influenza Vaccine

Trademarks not owned by the GlaxoSmithKline group of companies	Generic description
Fluzone® (Sanofi Pasteur)	Inactivated Trivalent Split Virion Influenza Vaccine

1. ETHICS

1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, any amendments, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational centre IEC or IRB.

1.2. Ethical conduct of the study

This study was conducted in accordance with ethical principles that have their origins in the Declaration of Helsinki, the principles of "good clinical practice" (GCP) and all applicable regulatory requirements.

1.3. Subject information and consent

Written informed consent was to be obtained from each subject's parent(s) / legally acceptable representative (LAR) prior to the performance of any study-specific procedures.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

GSK Biologicals was responsible for administration of the study, including clinical trial supply management and laboratory facilities for immunological testing.

The study was conducted in multicenters in the United States of America (USA).

The principal investigator was Joseph Domachowske, Department of Pediatrics, SUNY Upstate Medical Center, Syracuse, NY, USA.

3. INTRODUCTION

Influenza is a serious public health problem; it has a high incidence in the human population and causes regular large-scale morbidity and mortality. Children younger than 5 years of age have incidence rates of severe influenza disease and hospitalisation due to influenza second only to the elderly population.

Vaccination is currently the most effective means of controlling the impact of influenza in populations at risk.

Until recently, the prevailing immunization strategies for the prevention of seasonal influenza employ a trivalent influenza vaccine (TIV) which contains two A strains (H1N1 and H3N2) and a single B strain. However, since 1983, two evolutionarily distinct lineages of influenza B virus have co-circulated in the human population.

Because the two evolutionarily distinct lineages of influenza B virus continue to co-circulate, and cross-reactivity between the two lineages is low in a population with limited immunologic experience with influenza, an additional B strain antigen in the seasonal vaccine may offer broader protection to children [Englund, 2006; Hannoun, 2004; Heckler, 2007; Hobson, 1972; Levandowski, 1991].

GSK Biologicals' FLU Q-QIV, a split virion, inactivated, candidate quadrivalent influenza vaccine (QIV) consisting of four monovalent viral antigen bulks (prepared from influenza strains A/H1N1, A/H3N2, B/Victoria lineage and B/Yamagata lineage), has been studied in 600 children 6 to 35 months of age, given as a 0.5 mL dose in an open-label arm of the paediatric study FLU Q-QIV-003 and in a blinded group of the paediatric study, FLU Q-QIV-013 in which FLU Q-QIV was shown to be immunogenic, exceeding Center for Biologics Evaluation and Research (CBER)'s seroconversion rate (SCR) criterion for each strain, and had an acceptable safety profile with no notable differences compared to the licensed TIV control.

The purpose of this Phase II study was to obtain preliminary results by comparing FLU Q-QIV and a United States (US) licensed comparator*, Fluzone* (a split virion, inactivated, TIV influenza vaccine licensed in the US for use in persons 6 months of age and above) in children 6 to 35 months of age prior to a follow-up Phase III study. *Fluzone* was chosen as a comparator since it is currently the only TIV licensed in the US in children from 6 months old. This study has generated haemagglutination inhibition (HI) antibody response results (post-vaccination geometric mean titre [GMT] ratios and SCR differences) that are necessary to design an adequately powered Phase III study.

4. STUDY OBJECTIVES

4.1. Primary objective

- To assess the immunogenicity of FLU Q-QIV based on CBER's SCR criterion for each of the four strains in children 6 to 35 months of age, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively).

  Criterion for determination of effective immunization:

  - The lower limit (LL) of the two-sided 95% confidence interval (CI) for SCR should be ≥ 40% for each strain.

4.2. Secondary objectives

- To test the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of GMT and SCR) in all subjects approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively) by comparing FLU Q-QIV to *Fluzone*.

  Criteria to conclude superiority of the B/Victoria strain:

  Immunogenic superiority of the B/Victoria strain would be concluded if

  - The LL of the two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluzone*) was greater than 1.5, and
  - The LL of the two-sided 95% CI for the SCR difference (FLU Q-QIV minus *Fluzone*) was greater than 10%.
- To describe the immunogenicity (in terms of GMTs, seroprotection rates [SPRs], SCRs and mean geometric increases [MGIs]) of FLU Q-QIV and *Fluzone*.
- To describe the reactogenicity and safety of FLU Q-QIV and *Fluzone* in terms of:
  - Solicited local and general AEs during the 7-day post-vaccination follow-up period (day of vaccination and six subsequent days).
  - Unsolicited AEs during the 28-day post-vaccination follow-up period (day of vaccination and 27 subsequent days).
  - Serious adverse events (SAEs), medically attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period.
- To evaluate the relative risk of fever of FLU Q-QIV compared to *Fluzone* during a 4-day follow-up period.

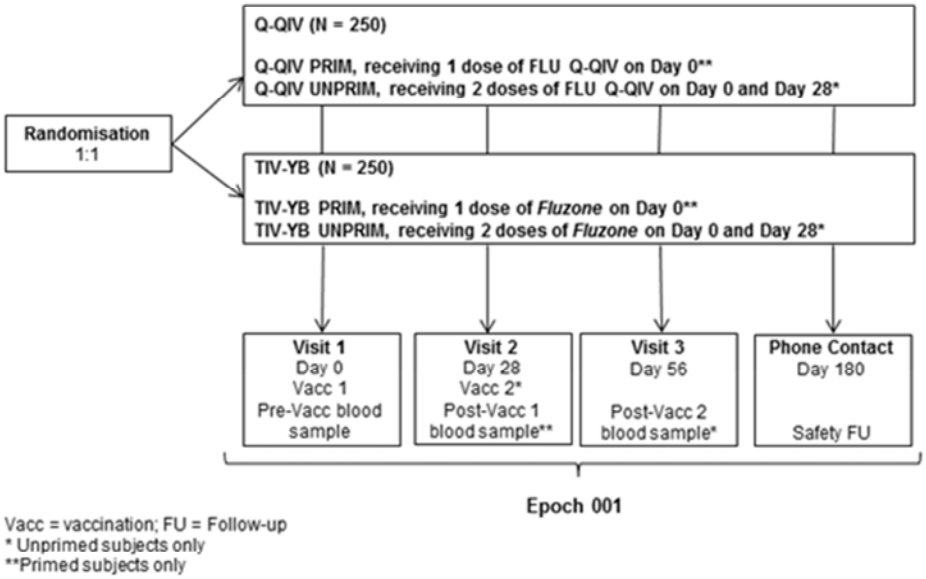
4.3. Tertiary objective

- To describe the GMT ratio and SCR difference of FLU Q-QIV vs *Fluzone* for the three common strains present in both vaccines:
  - GMT ratio (*Fluzone*/Q-QIV) with 95% CI
  - SCR difference (*Fluzone minus Q-QIV*) with 95% CI

5. INVESTIGATIONAL PLAN

5.1. Study design

5.1.1. Overall study design – Description



Refer to Section 5.12.2 for the change in the total number of subjects recruited.

- **Experimental design**: Phase II, observer-blind, randomised (1:1), controlled, parallel-group and multi-centre study.
- **Duration of the study**: Approximately 6 months for each enrolled subject to complete the study.
  - Epoch 001: Primary starting at Visit Day 0 and ending at Phone Contact Day 180.
- **Study groups:**

Table 1 Study groups and epochs foreseen in the study

Study Groups	Number of subjects	Age (Min – Max) (months)	Epochs
			Epoch 001
Q-QIV PRIM	250	6 months – 35 months	x
Q-QIV UNPRIM			
TIV-YB PRIM	250	6 months – 35 months	x
TIV-YB UNPRIM			

TIV = trivalent; QIV = quadrivalent; YB = Yamagata lineage B strain

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine name	Study Groups			
		Q-QIV PRIM	Q-QIV UNPRIM	TIV-YB PRIM	TIV-YB UNPRIM
Q-QIV	Flu-Q-QIV	x	x		
TIV-YB	*Fluzone*			x	x

- **Control**: active control (*Fluzone*)
- **Vaccination schedules**:
  - Primed* subjects: one intramuscular (IM) injection, on Day 0.
  - Unprimed* subjects: two IM injections, on Day 0 and on Day 28.

  *See GLOSSARY OF TERMS for the definitions of primed and unprimed subjects.
- **Treatment allocation**: Subjects were randomised 1:1 in the Q-QIV and TIV-YB groups.
  - Age (6 to 17 and 18 to 35 months), study centre, and the pre-study influenza vaccine priming status of the subjects were minimisation factors to ensure balanced representation of the combination of the minimisation factors in the two study groups.
- **Blinding**: observer-blind
- **Sampling schedule**: Blood samples were collected on Days 0 and 28 for primed subjects and on Days 0 and 56 for unprimed subjects.
- **Type of study**: self-contained
- **Data collection**: electronic Case Report Form (eCRF)

5.2. Study procedures

Table 3 and Table 4 summarise the list of study procedures during study visits and the final study contact for primed and unprimed subjects, respectively.

Table 3 List of study procedures for primed subjects – one vaccine dose

Age	6 to 35 months		
Epoch	Epoch 001		
Type of contact	visit 1	visit 2	phone contact
Time points	Day 0	Day 28	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	
Informed consent by parent(s)/LAR(s)	●		
Check inclusion/exclusion criteria	●		
Check elimination criteria		●	●
Check contraindications to vaccination	●		
Collect demographic data (including weight and height)	●		
Medical history	●		
History of influenza vaccination	●		
Physical examination (history directed)	●	● §	
Pre-vaccination body temperature	●		
Internet randomisation	●		
Blood sampling (approximately 4 mL) for humoral immune response determination	●	●	
Vaccine administration	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily (Days 0-6) and unsolicited AEs (Days 0-27)	O		
Return of diary cards		O	
Diary card transcription by investigator		●	
Record any concomitant medication/vaccination	●	●	●
Record any intercurrent medical conditions	●	●	●
Recording of SAEs	● #	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●
Recording of MAEs and pIMDs	●	●	●
Check willingness to participate in future trials			●
Study conclusion		●	●

LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; pIMDs = potential Immune-Mediated Diseases; SAE = Serious Adverse Event; Vacc = vaccination

● was used to indicate a study procedure that required documentation in the individual eCRF

○ was used to indicate a study procedure that did not require documentation in the individual eCRF

§ if deemed necessary by the investigator

Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

Table 4 List of study procedures for unprimed subjects – two vaccine doses

Age	6 to 35 months			
Epoch	Epoch 001			
Type of contact	visit 1	visit 2	visit 3	phone contact
Time points	Day 0	Day 28	Day 56	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	Post-Vacc 2	
Informed consent by parent(s)/LAR(s)	●			
Check inclusion/exclusion criteria	●			
Check elimination criteria		●	●	●
Check contraindications to vaccination	●	●		
Collect demographic data (including weight and height)	●			
Medical history	●			
History of influenza vaccination	●			
Physical examination (history directed)	●	● §	● §	
Pre-vaccination body temperature	●	●		
Internet randomisation	●	●		
Blood sampling (approximately 4 mL) for humoral immune response determination	●		●	
Vaccine administration	●	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily (Days 0-6) and unsolicited AEs (Days 0-27)	O	O		
Return of diary cards		O	O	
Diary card transcription by investigator		●	●	
Record any concomitant medication/vaccination	●	●	●	●
Record any intercurrent medical conditions	●	●	●	●
Recording of SAEs	● #	●	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●	●
Recording of MAEs and pIMDs	●	●	●	●
Check willingness to participate in future trials				●
Study conclusion			●	●

LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; pIMDs = potential Immune-Mediated Diseases; SAE = Serious Adverse Event; Vacc = vaccination

● was used to indicate a study procedure that required documentation in the individual eCRF

○ was used to indicate a study procedure that did not require documentation in the individual eCRF

§ if deemed necessary by the investigator

Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

Time intervals between study visits related to study procedures performed in subjects participating in the study are presented in Table 5.

Table 5 Intervals between study visits

Interval	Optimal length of interval [1]	Allowed interval [2]
Day 0 → Day 28	28 days	25 - 42 days
Day 28 → Day 56 *	28 days	25 - 42 days
Day 0 → Day 180	180 days	166 - 201 days

[1] Whenever possible the investigator had to arrange study visits within this interval.

[2] Subjects would not be eligible for inclusion in the ATP cohort for analysis of immunogenicity if they made the study visit outside this interval.

*Only applicable for unprimed subjects

5.3. Selection of study population

5.3.1. Inclusion criteria for enrolment

The study enrolled eligible subjects with stable health between the age of 6 and 35 months, as determined by the investigator's clinical examination and assessment of the subjects' medical history, and for whom the investigator determined that their parents/LARs could and would comply with the requirements of the protocol. Written informed consent was obtained from the parent(s)/LAR(s) of the subject.

5.3.2. Exclusion criteria

Criteria leading to the exclusion of subjects from the study included administration of an influenza vaccine or chronic use of immune-modifying drugs within 6 months prior to the first vaccine dose, any investigational or non-registered drug within 30 days prior to or during the study, and administration of immunoglobulins and/or any blood products within the three months before study entry. Subjects were also excluded if they had a history of any of the following: confirmed or suspected immunosuppressive or immunodeficient condition; history of Guillain-Barré syndrome within 6 weeks of receipt of prior inactivated influenza virus vaccine; any known or suspected allergy to any constituent of influenza vaccines; any significant disorder of coagulation or treatment with warfarin derivatives or heparin and any other condition which, in the opinion of the investigator, which would have prevented the subject from participating in the study. Children in care (see GLOSSARY OF TERMS) were not included in the study.

5.3.3. Withdrawal criteria

5.3.3.1. Subject completion

A subject who was available for the concluding contact foreseen in the protocol was considered to have completed the study.

5.3.3.2. Subject withdrawal from the study

From an analysis perspective, a 'withdrawal' from the study referred to any subject who was not available for the concluding contact foreseen in the protocol.

All data collected until the date of withdrawal/last contact of the subject was used for the analysis.

A subject was considered a 'withdrawal' from the study when no study procedure had occurred, no follow-up had been performed and no further information had been collected for this subject from the date of withdrawal/last contact.

Investigators were to make an attempt to contact those subjects who did not return for scheduled visits or follow-up.

Subjects who were withdrawn because of SAEs/AEs were clearly distinguished from subjects who were withdrawn for other reasons. Investigators were to follow subjects who were withdrawn as result of a SAE/AE until resolution of the event. Withdrawals were not replaced.

Information relative to the withdrawal was documented in the eCRF. The investigator documented whether the decision to withdraw a subject from the study was made by the subject's parent(s) or LAR(s), or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- SAE
- Non-serious AE
- Protocol violation (was to be specified)
- Consent withdrawal, not due to an AE*
- Moved from the study area
- Lost to follow-up
- Other (was to be specified)

*In case a subject was withdrawn from the study because the subject's parent(s)/LAR(s) withdrew consent, the investigator was to document the reason for withdrawal of consent, if specified, in the eCRF.

5.3.3.3. Subject withdrawal from investigational vaccine

A 'withdrawal' from the investigational vaccine referred to any subject who did not receive the complete treatment, i.e., when no further planned dose was administered from the date of withdrawal. A subject withdrawn from the investigational vaccine was not necessarily withdrawn from the study as further study procedures or follow-up may have been performed (safety or immunogenicity) if planned in the study protocol.

Information relative to premature discontinuation of the investigational vaccine was documented on the Vaccine Administration screen of the eCRF. The investigator documented whether the decision to discontinue further vaccination/treatment was made by the subject's parent(s) or LAR(s), or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- SAE
- Non-serious AE
- Other (was to be specified)

5.3.3.4. Elimination criteria

Administration of an influenza vaccine or immune-modifying drugs chronically administered or use of any investigational or non-registered drug other than the study

vaccine or administration of immunoglobulins and/or any blood products during the study period could determine a subject's evaluability in the ATP analysis. If subjects incurred a condition that had the capability of altering their immune response, they could be eliminated from the ATP cohort for immunogenicity. All intercurrent medical conditions (reported/ observed subsequent to the first vaccination) were to be recorded in the eCRF.

5.3.3.5. Contraindications to subsequent vaccination

The following events constituted absolute contraindications to further administration of FLU Q-QIV vaccine. If any of these events occurred during the study, the subject was not to receive additional doses of vaccine but could have continued other study procedures at the discretion of the investigator.

- Anaphylaxis following the administration of vaccine(s).

The following events constituted contraindications to administration of the study vaccines at that point in time; if any of these events occurred at the time scheduled for vaccination, the subject could have been vaccinated at a later date, within the time window specified in the protocol, or the subject could have been withdrawn at the discretion of the investigator.

- Acute disease and/or fever at the time of vaccination.
    - Fever was defined as temperature ≥ 38.0°C/100.4°F by any method.
    - Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever could be administered all vaccines.

5.4. Composition and administration of vaccine(s)

5.4.1. Description of vaccine(s)

The control vaccine (*Fluzone*) and the candidate vaccine (FLU Q-QIV) to be used were developed and manufactured by Sanofi Pasteur and GSK Biologicals, respectively, and had a thimerosal-free formulation.

Fluzone:

The TIV *Fluzone* vaccine contained HA from three influenza strains, with a total HA content of 22.5 µg, recommended for the influenza season 2013-2014 by the World Health Organisation (WHO), CDC/CBER, and European Medicines Agency (EMEA)/Committee for Medicinal Products for Human Use (CHMP):

- H1N1 strain: A/California/7/2009 (H1N1) (7.5 µg)
- H3N2 strain: A/Texas/50/2012 (H3N2) (7.5 µg)
- B strain (Yamagata lineage): B/Massachusetts/2/2012 (7.5 µg)

The excipients used in the *Fluzone* formulations complied with the United States and/or European Pharmacopoeia (see Table 6).

Commercial vaccines were assumed to have complied with the specifications given in the manufacturer's Summary of Product Characteristics (SPC).

FLU Q-QIV:

The FLU Q-QIV vaccine used in the trial had a total HA content of 60 µg.

It contained the same influenza A-like strains as those described for *Fluzone* above, as well as the most recently WHO, CDC/CBER, and EMEA/CHMP recommended B strains from the lineage included in the 2013-2014 WHO recommendations, i.e., B/Massachusetts/2/2012 (15 µg) and B/Brisbane/60/2008 (15 µg):

- H1N1 strain: A/California/7/2009 (H1N1) (15 µg)
- H3N2 strain: A/Texas/50/2012 (H3N2) (15 µg)
- B strain (Victoria lineage): B/Brisbane/60/2008 (15 µg)
- B strain (Yamagata lineage): B/Massachusetts/2/2012 (15 µg)

The excipients used in the FLU Q-QIV formulation complied with the United States and/or European Pharmacopoeia (see Table 6).

The Quality Control Standards and Requirements for the candidate vaccine were described in separate Quality Assurance documents (e.g. release protocols, certificate of analysis) and the required approvals had been obtained.

The tip caps of the prefilled syringes may have contained natural rubber latex which could cause allergic reactions in latex sensitive individuals; therefore latex was to be considered as a component of the vaccines.

The vaccines were labelled and packed according to applicable regulatory requirements.

Table 6 Study vaccines

Treatment name	Vaccine name	Formulation	Presentation	Volume	Number of doses	Lot number(s)
Q-QIV	Flu-Q-QIV	Sodium chloride, potassium chloride, sodium phosphate dibasic heptahydrate, potassium phosphate monobasic, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80) and water for injection	Translucent to off-white/greyish opalescent suspensions that may sediment slightly, presented in prefilled syringes	0.5 ml	1 (primed subjects) 2 (unprimed subjects)	DFLHA804A
TIV-YB	*Fluzone*	Sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde, octylphenol ethoxylate, gelatin	Clear and slightly opalescent presented in prefilled syringes	0.25 ml	1 (primed subjects) 2 (unprimed subjects)	DLOCA085A (U4694EA) DLOCA097A (U4694EA) DLOCA100A (U4711DA)

5.4.2. Dosage and administration of study vaccine(s)

Primed subjects received a single 0.5 mL dose of FLU Q-QIV or a single 0.25 mL dose of *Fluzone* administered IM on Day 0. Unprimed subjects received two 0.5 mL doses of FLU Q-QIV or two 0.25mL doses of *Fluzone* administered IM on Days 0 and 28.

The vaccines were to be administered as indicated in Table 7 (subjects < 12 months of age) and Table 8 (subjects ≥ 12 months of age).

Table 7 Dosage and administration for subjects below 12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route [1]	Site [2]	Side
Visit Day 0	0.5 ml	Q-QIV PRIM	Q-QIV	IM	Anterolateral thigh	Left
		Q-QIV UNPRIM				
Visit Day 28	0.5 ml	Q-QIV UNPRIM				
Visit Day 0	0.25 ml	TIV-YB PRIM	TIV-YB	IM	Anterolateral thigh	Left
		TIV-YB UNPRIM				
Visit Day 28	0.25 ml	TIV-YB UNPRIM				

[1]Intramuscular (IM)
[2]Thigh injection was the recommended route for subjects < 12 months, however the other route (deltoid) might have been considered based on the individual anatomy.

Table 8 Dosage and administration for subjects greater than or equal to 12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route [1]	Site [2]	Side[3]
Visit Day 0	0.5 ml	Q-QIV PRIM	Q-QIV	IM	Deltoid	Non-dominant
		Q-QIV UNPRIM				
Visit Day 28	0.5 ml	Q-QIV UNPRIM				
Visit Day 0	0.25 ml	TIV-YB PRIM	TIV-YB	IM	Deltoid	Non-dominant
		TIV-YB UNPRIM				
Visit Day 28	0.25 ml	TIV-YB UNPRIM				

[1]Intramuscular (IM)
[2]Deltoid injection was the recommended route for subjects ≥ 12 months, however the other route (thigh) might have been considered based on the individual anatomy.
[3]Or left arm if dominance was not yet identified

The vaccine recipients were to be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of the vaccine(s).

The contraindications to subsequent vaccination have been presented in Section 5.3.3.5 and warnings/precautions to vaccination were specified in the protocol (see protocol for details).

5.4.3. Treatment allocation and randomisation

5.4.3.1. Subject identification

Subject identification numbers were assigned sequentially to the subjects whose parent(s)/LAR(s) consented to participate in the study, according to the range of subject identification numbers allocated to each study centre.

5.4.3.2. Randomisation of treatment

5.4.3.2.1. Randomisation of supplies

The randomisation of supplies within blocks was performed at GSK Biologicals, using MATerial EXcellence (MATEX), a program developed for use in Statistical Analysis System (SAS®) (Cary, NC, USA) by GSK Biologicals. Entire blocks were shipped to the study centres /warehouse(s).

To allow GSK Biologicals to take advantage of greater rates of recruitment than anticipated at individual centres in this multi-centre study and to thus reduce the overall study recruitment period, an over-randomisation of 5% of supplies were to be prepared.

5.4.3.2.2. Study group and treatment number allocation

The treatment numbers were allocated by dose. Each dose had a single unique treatment number throughout the study.

The target was to enrol approximately 500 eligible subjects who would be randomly assigned to two study groups in a 1:1 ratio (approximately 250 subjects in each group).

Age (6 to 17 and 18 to 35 months), study centre, and the pre-study influenza vaccine priming status of the subjects were the minimisation factors to ensure balanced representation of the combination of the minimisation factors in the two study groups.

After obtaining the signed and dated ICF from the subject's parent(s)/LAR(s) and having checked the eligibility of the subject, the study staff in charge of the vaccine administration accessed SBIR. Upon providing the priming status, age and the subject identification number, the randomisation system determined the study group and provided the treatment number to be used for each dose.

The number of each administered treatment was recorded in the eCRF on the Vaccine Administration screen.

As soon as the target number of 500 subjects was reached, the enrolment was to be frozen.

5.4.3.2.3. Treatment number allocation for subsequent doses

For each dose subsequent to the first dose, the study staff in charge of the vaccine administration accessed SBIR, provided the subject identification number, and the system then provided a treatment number consistent with the allocated study group.

The number of each administered treatment was recorded in the eCRF on the Vaccine Administration screen

5.5. Blinding

Data was collected in an observer-blind manner. By observer-blind, it was meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g. safety and reactogenicity) were all unaware of which vaccine was administered. To do so, vaccine preparation and administration was to be done by authorised medical personnel who would not have participated in any of the study clinical evaluation assays.

The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample

5.6. Prior and concomitant medication /vaccinations

At each study visit/contact, the investigator was to question the subject's parent(s)/LAR(s) about any medication/product taken and vaccination received by the subject.

The following concomitant medications/products/vaccines were to be recorded in the eCRF if administered during the indicated recording period:

- All concomitant medications/products, except vitamins and dietary supplements, during the active study period, i.e., from Day 0 to 28 days after the last dose of study vaccine.
- Prophylactic medication was to be recorded as from 2 days before administration of the study vaccine to 28 days after the last dose of study vaccine.
- Any concomitant vaccination administered in the period starting 30 days before the first dose of study vaccine and ending at the last study contact.
- Any influenza vaccine within up to 6 months before the administration of study vaccine on Day 0 or at any time from Day 0 to study end.
- Any investigational medication or vaccine administered in the period starting 30 days before the administration of the study vaccine until the end of the study.
- Any concomitant medications/products/vaccines listed in Section 5.3.3.4.
- Any concomitant medication/product/vaccine relevant to an SAE* or administered at any time during the study period for the treatment of an SAE*.

* SAEs that were required to be reported per protocol.

5.7. Assessment of efficacy variables

Not applicable.

5.8. Assessment of immunogenicity variables

Table 9 presents the summary of immunogenicity assessments.

Table 9 Summary of immunogenicity assessments

Blood sample from Subjects	Assay	Assay cut-off	Contact and timepoint	Laboratory	Laboratory address
All	Influenza Virus A/California/7/2009 (H1N1).Hemagglutinin Ab: Hemagglutination Inhibition	10	Visit 1 Day 0	GSK Biologicals	GSK Biologicals Global Vaccine Clinical Laboratory, GSK (SSW) - Virology Zirkusstrasse, 40 - Dresden D-01069 - Germany
	Influenza Virus A/Texas/50/2012 (H3N2).Hemagglutinin Ab*: Hemagglutination Inhibition	10		GSK Biologicals	
	Influenza Virus B/Massachusetts/2/2012 (Yamagata).Hemagglutinin Ab: Hemagglutination Inhibition	10		GSK Biologicals	
	Influenza Virus B/Brisbane/60/2008 (Victoria).Hemagglutinin Ab: Hemagglutination Inhibition	10		GSK Biologicals	
Primed subjects	Influenza Virus A/California/7/2009 (H1N1).Hemagglutinin Ab: Hemagglutination Inhibition	10	Visit 2 Day 28	GSK Biologicals	GSK Biologicals Global Vaccine Clinical Laboratory, GSK (SSW) - Virology Zirkusstrasse, 40 - Dresden D-01069 - Germany
	Influenza Virus A/Texas/50/2012 (H3N2)*.Hemagglutinin Ab: Hemagglutination Inhibition	10		GSK Biologicals	
	Influenza Virus B/Massachusetts/2/2012 (Yamagata).Hemagglutinin Ab: Hemagglutination Inhibition	10		GSK Biologicals	
	Influenza Virus B/Brisbane/60/2008 (Victoria).Hemagglutinin Ab: Hemagglutination Inhibition	10		GSK Biologicals	
Unprimed subjects	Influenza Virus A/California/7/2009 (H1N1).Hemagglutinin Ab: Hemagglutination Inibition	10	Visit 3 Day 56	GSK Biologicals	GSK Biologicals Global Vaccine Clinical Laboratory, GSK (SSW) - Virology Zirkusstrasse, 40 - Dresden D-01069 - Germany
	Influenza Virus A/Texas/50/2012 (H3N2).Hemagglutinin Ab*: Hemagglutination Inhibition	10		GSK Biologicals	
	Influenza Virus B/Massachusetts/2/2012 (Yamagata).Hemagglutinin Ab: Hemagglutination Inhibition	10		GSK Biologicals	
	Influenza Virus B/Brisbane/60/2008 (Victoria).Hemagglutinin Ab: Hemagglutination Inhibition	10		GSK Biologicals	

*A/Texas/50/2012 is an A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011

5.8.1. Immunological correlates of protection

Although no generally accepted immunological correlate of protection has been demonstrated so far against influenza with respect to specific levels of HA-specific antibody titre post-vaccination induced with inactivated influenza virus vaccines, the protective role of antibodies against HA and, to a lesser extent, neuraminidase, is well established and has been demonstrated both in experimentally infected animals and humans [Brydak, 2000]. For this reason, the induction of antibodies is used as marker of potential vaccine efficacy and the serum HI assay is used to demonstrate this humoral response. HI antibody titres of 1:40 or greater have been associated with protection from influenza illness in at least 50% of adult subjects in some human challenge studies [Hannoun, 2004; Hobson, 1972]. While the 1:40 titre is termed "seroprotection" for convenience, it is recognised that no association of this titre with protection has been formally demonstrated in children.

5.9. Assessment of safety variables

The standard definitions for AE and SAE are provided in the Protocol.

5.9.1. Solicited adverse events

Solicited AEs occurring during the 7-day follow-up period after vaccination were recorded. Solicited local (injection-site) and general AEs to be recorded are summarised in Table 10 and Table 11, respectively.

5.9.1.1. Solicited local (injection-site) adverse events

The following local (injection-site) AEs were solicited:

Table 10 Solicited local adverse events

Pain at injection site
Redness at injection site
Swelling at injection site

5.9.1.2. Solicited general adverse events

The following general AEs were solicited:

Table 11 Solicited general adverse events

Drowsiness
Fever
Irritability/Fussiness
Loss of appetite

5.9.2. Clinical laboratory parameters and other abnormal assessments qualifying as adverse events or serious adverse events

In absence of diagnosis, abnormal laboratory findings (e.g. clinical chemistry, haematology, urinalysis) or other abnormal assessments (e.g. physical examination findings) that were judged by the investigator to be clinically significant were to be recorded as AE or SAE if they met the definition of an AE or SAE. Clinically significant abnormal laboratory findings or other abnormal assessments that were present at baseline and significantly worsened following the start of the study were also to be reported as AEs or SAEs. However, clinically significant abnormal laboratory findings or other abnormal assessments that were associated with the disease being studied, unless judged by the investigator as more severe than expected for the subject's condition, or that were present or detected at the start of the study and did not worsen, were not to be reported as AEs or SAEs.

The investigator was to exercise his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment was clinically significant.

5.9.3. Adverse events of specific interest

5.9.3.1. Potential immune-mediated diseases

PIMDs are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. AEs that were to be recorded and reported as pIMDs included those listed in Table 12.

However, the investigator was to exercise his/her medical and scientific judgement in deciding whether other diseases had an autoimmune origin (i.e., pathophysiology involving systemic or organ-specific pathogenic autoantibodies). If so, these were to have also been recorded as a pIMD.

Table 12 List of potential immune-mediated diseases

Neuroinflammatory disorders	Musculoskeletal disorders	Skin disorders
• Cranial nerve disorders, including paralyses/paresis (e.g. Bell's palsy) • Optic neuritis • Multiple sclerosis • Transverse myelitis • Guillain-Barré syndrome, including Miller Fisher syndrome and other variants • Acute disseminated encephalomyelitis, including site specific variants: e.g. non-infectious encephalitis, encephalomyelitis, myelitis, myeloradiculomyelitis • Myasthenia gravis, including Lambert-Eaton myasthenic syndrome • Immune-mediated peripheral neuropathies and plexopathies, (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy). • Narcolepsy	• Systemic lupus erythematosus • Scleroderma, including diffuse systemic form and CREST syndrome • Systemic sclerosis • Dermatomyositis • Polymyositis • Antisynthetase syndrome • Rheumatoid arthritis, • Juvenile chronic arthritis, (including Still's disease) • Polymyalgia rheumatic • Spondyloarthritis, including ankylosing spondylitis, reactive arthritis (Reiter's Syndrome) and undifferentiated spondyloarthritis • Psoriatic arthropathy • Relapsing polychondritis • Mixed connective tissue disorder	• Psoriasis • Vitiligo • Erythema nodosum • Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis) • Cutaneous lupus erythematosus • Alopecia areata • Lichen planus • Sweet's syndrome • Morphoea

Liver disorders	Gastrointestinal disorders	Metabolic diseases
• Autoimmune hepatitis • Primary biliary cirrhosis • Primary sclerosing cholangitis • Autoimmune cholangitis	• Crohn's disease • Ulcerative colitis • Ulcerative proctitis • Celiac disease	• Autoimmune thyroiditis (including Hashimoto thyroiditis) • Grave's or Basedow's disease • Diabetes mellitus type I • Addison's disease

Vasculitides	Others
• Large vessels vasculitis including: giant cell arteritis such as Takayasu's arteritis and temporal arteritis. • Medium sized and/or small vessels vasculitis including: polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg–Strauss syndrome (allergic granulomatous angiitis), Buerger's disease (thromboangiitis obliterans), necrotizing vasculitis and anti-neutrophil cytoplasmic antibody (ANCA) positive vasculitis (type unspecified), Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis.	• Autoimmune hemolytic anemia • Autoimmune thrombocytopenia • Antiphospholipid syndrome • Pernicious anemia • Autoimmune glomerulonephritis (including IgA nephropathy, glomerulonephritis rapidly progressive, membranous glomerulonephritis, membranoproliferative glomerulonephritis, and mesangioproliferative glomerulonephritis) • Uveitis • Autoimmune myocarditis/cardiomyopathy • Sarcoidosis • Stevens-johnson syndrome • Sjögren's syndrome • Idiopathic pulmonary fibrosis • Goodpasture syndrome • Raynaud's phenomenon

Note: This list was based on the Medical Dictionary for Regulatory Activities (MedDRA), Version 16.0. The data cleaning and analysis for pIMDs was to be adjusted accordingly if the MedDRA dictionary for pIMDs was updated.

5.9.4. Time period for detecting and recording adverse events and serious adverse events

All AEs starting within 28 days following administration of each dose of study vaccine/comparator was recorded into the appropriate section of the eCRF, irrespective of intensity or whether or not they were considered vaccination-related.

The time period for collecting and recording SAEs, MAES and pIMDs began at the first receipt of study vaccine/comparator and ended 180 days following administration of the first dose of study vaccine/comparator for each subject.

All AEs/SAEs leading to withdrawal from the study were collected and recorded from the time of the first receipt of study vaccine/comparator until the end of the study.

In addition to the above-mentioned reporting requirements and in order to fulfil international reporting obligations, SAEs that were related to study participation (i.e., protocol-mandated procedures, invasive tests, a change from existing therapy) or were related to a concurrent GSK medication/vaccine were collected and recorded from the time the subject consented to participate in the study until she/he was discharged from the study.

An overview of the protocol-required reporting periods for AEs and SAEs, is given in Table 13.

Table 13 Reporting periods for adverse events and serious adverse events

Event	Pre-Vacc*	Vacc 1	7 days post-Vacc 1	28 days post-Vacc 1	Vacc 2**	6 days post-Vacc 2**	28 days post-Vacc 2**	6 months post-Vacc 1
Time point		Day 0	Day 6	Day 27	Day 28	Day 34	Day 56	Day 180
Solicited local and general AEs								
Unsolicited AEs								
AEs/SAEs leading to withdrawal from the study								
SAEs related to study participation or concurrent GSK medication/vaccine								
SAEs, MAEs, pIMDs								
Recording of intercurrent medical conditions								

Vacc = vaccination; Pre-Vacc = pre-vaccination; (S)AE = (Serious) Adverse Event; pIMD = potential Immune-Mediate Disease; MAE = Medically Attended Adverse Event
*Informed consent obtained
**Only for unprimed subject

5.9.5. Post-Study adverse events and serious adverse events

A post-study AE/SAE was defined as any event that occurred outside of the AE/SAE reporting period defined in Table 13. Investigators were not obligated to actively seek AEs or SAEs in former study participants. However, if the investigator learnt of any SAE at any time after a subject had been discharged from the study, and he/she considered the event reasonably related to the investigational vaccine/product, the investigator was to promptly notify the Study Contact for Reporting SAEs.

5.9.6. Assessment of adverse events

5.9.6.1. Assessment of intensity

The intensity of the following solicited AEs was assessed as described:

Table 14 Intensity scales for solicited symptoms in infants/toddlers and children

Infant/Toddler (15–24 months)/Child		
Adverse Event	**Intensity grade**	**Parameter**
Pain at injection site	0	None
	1	Mild: Minor reaction to touch
	2	Moderate: Cried/protested on touch
	3	Severe: Cried when limb was moved/spontaneously painful
Redness at injection site		Recorded greatest surface diameter in mm
Swelling at injection site		Recorded greatest surface diameter in mm
Fever*		Recorded temperature in °C/°F
Irritability/Fussiness	0	Behaviour was as usual
	1	Mild: Crying was more than usual/no effect on normal activity
	2	Moderate: Crying was more than usual/interfered with normal activity
	3	Severe: Crying that could not be comforted/prevented normal activity
Drowsiness	0	Behaviour was as usual
	1	Mild: Drowsiness was easily tolerated
	2	Moderate: Drowsiness that interfered with normal activity
	3	Severe: Drowsiness that prevented normal activity
Loss of appetite	0	Appetite was as usual
	1	Mild: Ate less than usual/no effect on normal activity
	2	Moderate: Ate less than usual/interfered with normal activity
	3	Severe: Did not eat at all

*Fever was defined as temperature ≥ 38.0°C / 100.4°F by any method

The maximum intensity of local injection site redness/swelling was scored at GSK Biologicals as follows:

0	:	≤ 20 mm
1	:	> 20 - ≤ 50 mm
2	:	> 50 - ≤ 100 mm
3	:	> 100 mm

The grade of fever was scored as follows:

1	:	≥ 38.0°C (100.4°F) - ≤ 38.5°C (101.3°F)
2	:	> 38.5°C (101.3°F) - ≤ 39.0°C (102.2°F)
3	:	> 39.0°C (102.2°F) - ≤ 40.0°C (104°F)
4	:	> 40.0°C (104°F)

The investigator was to assess the maximum intensity that occurred over the duration of the event for all unsolicited AEs (including SAEs) recorded during the study. The assessment was based on the investigator's clinical judgement.

The intensity was assigned to one of the following categories:

1 (mild)	=	An AE which was easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE which was sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE which prevented normal, everyday activities (in a young child, such an AE would have, for example, prevented attendance at kindergarten/a day-care centre and would have caused the parent(s)/LAR(s) to seek medical advice.)

5.9.6.2. Assessment of causality

The investigator was obligated to assess the relationship between investigational vaccine/product and the occurrence of each AE/SAE. The investigator was to use clinical judgement to determine the relationship. Alternative plausible causes for the AE/SAE, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational vaccine were to be considered and investigated. The investigator was also to consult the IB and/or PI for marketed products to determine his/her assessment.

In case of concomitant administration of multiple vaccines/products, it may not have been possible to determine the causal relationship of general AEs to the individual vaccines administered. The investigator was to, therefore, assess whether the AE could have been causally related to vaccination rather than to the individual vaccines.

All solicited local (injection site) reactions were considered causally related to vaccination. Causality of all other AEs were to be assessed by the investigator using the following question:

Was there a reasonable possibility that the AE may have been caused by the investigational vaccine?

YES	:	There was a reasonable possibility that the vaccine(s) contributed to the AE.
NO	:	There was no reasonable possibility that the AE was causally related to the administration of the study vaccine(s). There were other, more likely causes and administration of the study vaccine(s) was not suspected to have contributed to the AE.

If an event met the criteria to be determined as 'serious', additional examinations/tests were to be performed by the investigator in order to determine ALL possible contributing factors for each SAE.

Possible contributing factors included:

- Medical history.
- Other medication.
- Protocol required procedure.
- Other procedure not required by the protocol.
- Lack of efficacy of the vaccine, if applicable.
- Erroneous administration.
- Other cause (was to be specified).

5.9.6.3. Assessment of outcomes

The investigator assessed the outcome of all unsolicited AEs (including SAEs) recorded during the study as:

- Recovered/resolved.
- Recovering/resolving.
- Not recovered/not resolved.
- Recovered with sequelae/resolved with sequelae.
- Fatal (SAEs only).

5.9.6.4. Medically attended visits

For each solicited and unsolicited symptom the subject experienced, the subject's parent(s)/LAR(s) was\were asked if the subject received medical attention defined as hospitalisation, or an otherwise unscheduled visit to or from medical personnel for any reason, including emergency room visits. This information was recorded in the eCRF

5.9.7. Follow-up of adverse events and serious adverse events

5.9.7.1. Follow-up during the study

After the initial AE/SAE report, the investigator was required to proactively follow each subject and provide additional relevant information on the subject's condition to GSK Biologicals (within 24 hours for SAE).

All SAEs, MAEs and pIMDs (serious or non-serious) documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were to be reviewed at subsequent visits/contacts until the end of the study.

With the exception of SAEs, MAEs and pIMDs, all AEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were to be reviewed at subsequent visits/contacts until 28 days after the last vaccination.

5.9.7.2. Follow-up after the subject was discharged from the study

The investigator was to follow subjects:

- with SAEs, pIMDs (serious or non-serious), or subjects withdrawn from the study as a result of an AE, until the event had resolved, subsided, stabilised, disappeared, or until the event was otherwise explained, or the subject was lost to follow-up.
- with MAEs, until the end of the study or the subjects were lost to follow-up.
- with other non-serious AEs, until Day 28 (primed subjects) or Day 56 (unprimed subjects) or they were lost to follow-up.

If the investigator received additional relevant information on a previously reported SAE, he/she was to provide this information to GSK Biologicals using a paper SAE report as applicable.

5.10. Statistical methods

The statistical analyses were performed using the Statistical Analysis Systems (SAS) version 9.2 on windows and StatXact-8.1 procedure for SAS.

5.10.1. Primary endpoint(s)

- Humoral immune response to each strain of FLU Q-QIV. Serum HI antibodies on Day 0 and 28 days after the last vaccine dose were used to calculate:

- SCRs

5.10.2. Secondary endpoints

- Humoral immune response against the B/Victoria strain. Serum HI antibody titres for the B/Victoria strain 28 days after the last vaccine were used to calculate:
  - GMT ratio (Q-QIV/*Fluzone*)
  - SCR difference (Q-QIV minus *Fluzone*)
- Humoral immune response to each strain. Serum HI antibody titres on Day 0 and 28 days after the last vaccine from both vaccine groups were used to calculate:
  - GMTs
  - SCRs
  - SPRs
  - MGIs
- Solicited local and general AEs
  - Occurrence of solicited local and general AEs (summarised by incidence rate, duration, intensity and relationship to vaccination [general AEs]) during a 7-day follow-up period (i.e., day of vaccination and six subsequent days) after each vaccination, in each group.
- Unsolicited AEs
  - Occurrence of unsolicited AEs (summarised by incidence rate, intensity, and relationship to vaccination) during a 28-day follow-up period (i.e., day of vaccination and 27 subsequent days) after each vaccination, in each group.
- MAEs, SAEs, and pIMDs
  - Occurrence of MAEs, SAEs and pIMDs (summarised by incidence rate and relationship to vaccination) during the entire study period.
- Occurrence of any fever (≥ 38°C) or grade 3 fever or higher (> 39°C) during a 4-day follow-up period after Dose 1 or Dose 2

5.10.3. Tertiary endpoints

- Humoral immune response against the three common strains. Serum HI antibody titres 28 days after the last vaccine were used to calculate (for the three common strains):
  - GMT ratio (*Fluzone*/Q-QIV)
  - SCR difference (*Fluzone minus Q-QIV*)

5.10.4. Determination of sample size

5.10.4.1. Primary objective

The primary objective was statistically powered to assess the immunogenicity of SCRs in children 6 to 35 months of age who received the FLU Q-QIV vaccine.

Table 15 shows the statistical power to meet CBER immunogenicity criterion in terms of SCR (LL of 95% of SCR > 40%).

Table 15 Power to meet CBER criterion in SCRs for immunogenicity for FLU Q-QIV

Endpoint (SCR)	Reference value[1] (SCR)	Power[2] to reject H0: SCR ≤ 40%
		N = 50
A/California/7/2009 (H1N1)	85.9%	>99.99%
A/Texas/50/2012 (H3N2)	72.2%	99.54%
B/Massachusetts/2/2012 (Yamagata)	78.9%	99.99%
B/Brisbane/60/2008 (Victoria)	73.9%	99.81%
Overall[3]		99.34%

[1] Observed SCRs in Q-QIV group from Study FLU-Q-QIV-013 (for children 6 to 35 months of age)
[2] Pass 2005, one-sided inequality test on proportion, alpha=2.5%
[3] Using Bonferroni adjustment on Type 2 error (beta)

Hence, with 50 evaluable subjects in the Q-QIV group, an overall power of 99.34% was to be reached to meet CBER criterion (SCR) simultaneously for all four strains.

The study planned to enrol 250 subjects per group (a total of 500 subjects) in order to assess the SCR difference between the two study groups, to detect any fever and grade 3 or higher fever. However, due to recruitment issues only 314 subjects (158 in the Flu Q-QIV group and 156 in the *Fluzone* group) were recruited in the study and this was sufficient to assess the primary objective (as only 50 subjects per group were). The primary reason for evaluating these objectives was to obtain preliminary data for the Phase III study with this product.

In this study, the primary immunogenicity objective was powered with a pre-specified criterion. The secondary confirmatory immunogenicity objective was planned to be evaluated if the primary immunogenicity objective was met.

5.10.4.2. Secondary objectives

5.10.4.2.1. Superiority of the B strain

Table 16 shows the power to demonstrate superiority of FLU Q-QIV to *Fluzone* in terms of B/Victoria antibody GMT with 50 evaluable children 6 to 35 months of age in each group.

Table 16 Power to detect superiority in HI antibody GMTs between FLU Q-QIV and *Fluzone* for B/Victoria strain

Endpoint (GMT)	Reference value		Power[3] to reject H0: GMT ratio (FLU Q-QIV/*Fluzone*) ≤ 1.5
	Standard Deviation of log_{10} transformed titre[1]	GMT ratio (FLU Q-QIV/*Fluzone*)[2]	N = 50 in each group
B/Brisbane/60/2008 (Victoria)	0.72	7.14	99.17%

[1] Standard deviation of log (titres) observed in the FLU-Q-QIV-013
[2] Reference GMT value=111.4 from Q-QIV group; and GMT=15.6 from D-TIV-YB in Study Q-QIV-013.
[3] Pass 2005, superiority test on means, alpha = 2.5%; equivalence margin = | log_{10}(1.5) |

Table 17 shows the power to demonstrate superiority in the B/Victoria strain SCRs between FLU Q-QIV and *Fluzone* on Day 28, with 50 evaluable children 6 to 35 months of age in each group.

Table 17 Power to detect superiority in SCRs between FLU Q-QIV and *Fluzone* for B/Victoria strain

Endpoint (SCR)	Number of evaluable subjects in each group	SCR[1]	SCR[1]	Power[2] to reject H0: difference in SC rates (FLU Q-QIV minus *Fluzone*) ≤ 10%
B/Brisbane/60/2008 (Victoria)	50	73.9%	9.8%	> 99.99%

[1] References SCR = 73.9% from Q-QIV group; and SCR = 9.8% from D-TIV-YB group in study FLU Q-QIV-013
[2] Power estimated using PASS, One-Sided exact test on the difference of proportions, H0: $\Delta \leq 0.1$, alpha = 2.5%.

The superiority of the B strain was to be concluded if the above both null hypotheses were rejected.

5.10.5. Study cohorts /data sets analyzed

5.10.5.1. Total vaccinated cohort

The Total vaccinated cohort (TVC) included all vaccinated subjects for whom data was available. For the total analysis of safety, this included all vaccinated subjects for whom safety data was available. For the total analysis of immunogenicity, this included vaccinated subjects for whom data concerning immunogenicity endpoint measures was available.

The TVC analysis was to be performed per treatment actually administered.

5.10.5.2. According-to-protocol cohort for analysis of safety

The ATP cohort for analysis of safety included all vaccinated subjects:

- Who had received at least one dose of study vaccine/comparator according to their random assignment

- With sufficient data to perform an analysis of safety
- Who did not meet any of the criteria for elimination from an ATP analysis during the study
- For whom administration site of study vaccine/comparator was known
- Who had not received a vaccine not specified or forbidden in the protocol

5.10.5.3. According-to-protocol cohort for analysis of immunogenicity

The ATP cohort for analysis of immunogenicity, in terms of antibody response measured by the HI assay, included all evaluable subjects (i.e.,, those meeting all eligibility criteria, complying with the procedures and intervals defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity endpoint measures was available. Therefore, this included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after vaccination and

- Who complied with their vaccine schedule (had received one dose for primed subjects; and had received two doses for unprimed subjects)
- Who complied with the procedures and intervals defined in the protocol
- Who did not meet any of the criteria for elimination from an ATP analysis
- Who did not receive a product leading to elimination from an ATP analysis
- Who did not present with a medical condition leading to elimination from an ATP analysis

The intervals between visits/contacts were to be strictly followed. These intervals determined each subject's eligibility to be included in the 'according to protocol' analyses.

5.10.6. Derived and transformed data

- **Immunogenicity**
  - The cut-off value was defined by the laboratory before the analysis and is described in Section 5.8.
  - A seronegative subject was a subject whose titre was below the cut-off value. A seropositive subject was a subject whose titre was greater than or equal to the cut-off value. For this study, HI titres of < 1:10 were considered below the cut-off.
  - The GMT calculations were performed by taking the anti-log of the mean of the log (base 10) transformed inverse titres (the number X denoted the inverse of a titre expressed as "1:X"). Antibody titres below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation.
  - SCR was defined as the incidence rate of vaccinees who have either a pre-vaccination (Day 0) titre recorded as < 1:10 for HI and a post-vaccination

titre ≥ 1:40 or a pre-vaccination titre ≥ 1:10 and at least a 4-fold increase in post-vaccination reciprocal titre.

- Seroprotection (SPR) was defined as the percentage of subjects who had a serum anti-HI antibody titre ≥1:40.
- MGI was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre. MGIs were calculated on Day 28 following the complete vaccination regimen.
- Handling of missing data: for a given subject and a given immunogenicity measurement, missing or non-evaluable measurements were not replaced. Therefore, analyses excluded subjects with missing or non-evaluable measurements.

- **Reactogenicity and Safety**
  - Incidence rates of AEs were calculated as the number of subjects who experienced the event, divided by the number of subjects in the safety analysis cohort (the TVC or ATP for safety analysis cohort).
  - Handling of missing data: For a given subject and the analysis of solicited AEs within 7 days post-vaccination (Days 0 through 6), missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited AEs based on the TVC included only vaccinated subjects and doses with documented safety data (i.e., symptom screen/sheet completed). Details of calculation of percentages of subjects with solicited or unsolicited AEs, as a percentage of doses or per subject, were contained in the Study Analysis Plan (SAP).
  - For the analysis of unsolicited AEs/MAEs/SAEs/concomitant medications, all vaccinated subjects were considered and subjects who did not report an event were considered as subjects without an event.
  - For summaries reporting both solicited and unsolicited AEs, all vaccinated subjects were considered in the TVC analysis. Subjects who did not report the event were considered as subjects without the event.
  - Relative risk of subjects with any fever or grade 3 or higher fever within 4 days post-vaccination was calculated between groups with the 95% CI derived using exact method for all subjects and by age stratum.

5.10.7. Analysis of demographics and other baseline characteristics

Demographic characteristics (age, height, weight, gender and race) of each study vaccine group were tabulated for all subjects by age stratum and priming status. No formal statistical evaluation of study group differences in demographic characteristics was performed.

Summary statistics for subjects' age, classified by gender of the vaccinated subjects as a whole, and per study group, were calculated.

The distribution of subjects enrolled among the study sites was tabulated as a whole and per group, and classified subjects into disposition categories, including subjects who entered, completed, or withdrew from the study. In addition, the number of subjects in each analysis population was presented. The number of subjects who received the vaccine was tabulated. Subjects who were screened but ineligible, as well as those who were excluded from the various analysis sets, were listed in the by-subject data listings.

The proportion of subjects with prior immunologic experience with influenza vaccine(s) in the previous three influenza seasons was tabulated for each study group and categorised by priming status (primed vs unprimed subjects).

5.10.8. Analysis of immunogenicity

The primary analysis was based on the ATP cohort for analysis of immunogenicity. Since the percentage of vaccinated subjects excluded from the ATP cohort for analysis of immunogenicity was more than 5%, a second analysis based on the TVC was performed to complement the ATP analysis.

5.10.8.1. Within groups assessment

To assess the humoral response in terms of HI antibodies for all vaccine strains, the following parameters (with 95% CI) were calculated by group for all subjects, each age strata (6 to 17 and 18 to 35 months of age) and by priming status (primed and unprimed):

- SCR, 28 days following last vaccination (primary endpoint)
- GMT of HI on Day 0 and 28 days following last vaccination
- MGI, 28 days following last vaccination
- SPR on Day 0 and 28 days following last vaccination

5.10.8.2. Between groups assessment

GMT ratio and SCR difference:

To assess the immunogenic superiority of the B/Victoria strain:

- The GMT ratio of FLU Q-QIV over *Fluzone* and the two-sided 95% CI was calculated.

- Difference of SCR (FLU Q-QIV minus *Fluzone*) and the 95% CI was calculated.

The superiority of FLU Q-QIV over *Fluzone* would be concluded if the LL of two-sided 95% CI of the GMT ratio (FLU Q-QIV/*Fluzone*) was > 1.5 and the LL of two-sided 95% CI on the SCR difference (FLU Q-QIV minus *Fluzone*) was > 10%.

To assess the immunogenic difference between FLU Q-QIV and *Fluzone* for the three common strains (H1N1, H3N2 and B/Yamagata), descriptively:

- The GMT ratio of *Fluzone* over FLU Q-QIV (*Fluzone*/FLU Q-QIV) and the two-sided 95% CI were calculated.
- The difference of SCR (*Fluzone* minus FLU Q-QIV) and the two-sided 95% CI were calculated.

5.10.9. Analysis of safety

The primary analysis was performed on the TVC. As the percentage of subjects excluded from the ATP cohort for analysis of safety was less than 5%, a second analysis was not performed on this ATP cohort.

Please refer to Section 5.12.2 for the change in analyses as planned in the protocol.

5.10.9.1. Within groups assessment

- The percentage of subjects with at least one local AE (solicited only), with at least one general AE (solicited only) and with any AE during the 7-day follow-up period was tabulated with exact 95% CI after each vaccine dose and overall. The percentage of doses followed by at least one local AE (solicited only), by at least one general AE (solicited only) and by any AE during the defined follow-up period was tabulated with exact 95% CI. The same calculations were performed for AEs rated as grade 3, related AEs and grade 3 related AEs.
- The percentage of subjects reporting each individual solicited local (any, grade 3, and medically attended) and general (any, grade 3, related, grade 3 related, and medically attended) AE during the 7-day solicited follow-up period was tabulated with exact 95% CI. The percentage of doses followed by each individual solicited local and general AE during the 7-day solicited follow-up period was tabulated with exact 95% CI.
- The verbatim reports of unsolicited AEs were reviewed by a physician and the signs and symptoms were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) Dictionary for Adverse Reaction Terminology. The percentage of subjects with at least one report of AE classified by MedDRA and reported up to 27 days after vaccination was tabulated with exact 95% CI. The same tabulations were performed for grade 3 unsolicited AEs, for unsolicited AEs with a relationship to vaccination and grade 3 unsolicited AEs with relationship to vaccination.
- MAEs, SAEs and pIMDs were collected and summarised through the entire follow-up period (180 days). In addition, SAEs and withdrawal due to AEs were described in detail.

5.10.9.2. Between groups assessment (Exploratory Analysis)

As an exploratory analysis, relative risk of subjects with any fever (≥ 38°C) and grade 3 (> 39°C) or higher fever during 4 days follow-up after vaccination(s) from two vaccine groups was calculated for all subjects along with the 95% CI. However, these results (relative risks) are to be interpreted with caution as there are no multiplicity adjustments made.

5.10.10. Sequence of analyses

One final analysis was performed on cleaned data at the end of the study (following the 6 month safety follow-up).

Please refer to Section 5.12.2 for the change in the sequence of analyses as planned in the protocol.

5.10.11. Interim analysis

There was no interim analysis, all analyses were conducted on final data and therefore no statistical adjustment for multiple analyses was required.

5.11. Data quality assurance at study level

To ensure that the study procedures conformed across all investigator sites, the protocol, electronic case report form and safety reporting were reviewed with the investigator(s) and his/her/their personnel responsible for the conduct of the study by the Company representative(s) prior to study start. A multi-investigator meeting was held prior to the study start.

Adherence to the protocol requirements and verification of data generation accuracy were achieved through monitoring visits to each investigator site. Computer checks and blinded review of subject tabulations were performed to ensure consistency of eCRF completion. All procedures were performed according to methodologies detailed in GlaxoSmithKline Vaccines Standard Operating Procedures (SOPs).

All protocol deviations collected during the study were reviewed by the GSK study team in order to identify important protocol deviations. Consistent with ICH E3 guidance, important deviations are defined as deviations that were likely to affect the interpretation of the results and/or led to exclusion of any subject data from an analysis. Important deviations include, but are not limited to, those related to study inclusion or exclusion criteria, adherence to the protocol, conduct of the study, subject management or subject assessment.

Independent Audit statement:

- No study specific audits were performed for this study.

5.12. Changes in the conduct of the study or planned analyses

5.12.1. Protocol amendments

The protocol dated 11 July 2013 was amended (Amendment 1, dated 07 October 2013) due to the following reason:

The original study protocol defined primed subjects (6 to 35 months of age) as those who had previously received two doses of seasonal influenza vaccine separated by at least one

month during the last season or who had received at least one dose prior to the last season. Due to their priming status, these subjects would have received only one dose of influenza vaccine in the current study. Unprimed subjects (6 to 35 months of age) were defined in the original protocol as those who had not received any seasonal influenza vaccine in the past or received only one dose for the first time in the last season and, therefore, these subjects would have received two doses (28 days apart) of vaccine in the study.

The United States Advisory Committee on Immunization Practices (ACIP) guidelines for the 2013-14 season (which was released after) defined primed subjects (6 months to 8 years of age) as children who have received a total of two or more doses of seasonal influenza vaccine since 01 July 2010 and these children would receive one dose of seasonal influenza vaccine in this study. All other children (6 months to 8 years of age) would be considered unprimed and would be given two doses of seasonal influenza vaccine 28 days apart.

This difference in the definition could have resulted in potential under-dosing (with the possible consequence of reduced vaccine efficacy) of some children 6 to 35 months of age who would be participating in the study.

Therefore, the definitions of primed and unprimed subjects (6 to 35 months of age) were changed to harmonize with the 2013-14 ACIP guidelines in order to ensure the recommended ACIP dosing schedule and to avoid potential inadequate dosing.

5.12.2. Other changes

Analyses were performed as planned in the protocol except for the following changes:

- Two clinical study reports (CSRs) were planned to be written (main CSR after Day 56 analysis and annex report after analysis of the 6 month follow-up) in the protocol. A statistical analysis was performed after Day 56 results; however, a decision was made to re-do a final analysis and generate only one final CSR at the end of 6 month follow-up period based on CBER feedback.
- According to the protocol and SAP, the percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE during the 7-day follow-up period was to be tabulated with exact 95% CI after each vaccine dose and overall. The percentage of doses followed by at least one local AE (solicited and unsolicited), by at least one general AE (solicited and unsolicited) and by any AE during the defined follow-up period was to be tabulated with exact 95% CI. The same calculations were to be performed for AEs rated as grade 3, related AEs and grade 3 related AEs. As per the feedback from CBER, only solicited AEs (instead of solicited and unsolicited AEs) during the 7-day follow up period have been tabulated in this reported.
- Due to ARGUS migration, SAEs were collected only in the clinical database.
- Due to non-participation of Mexico in the study (a site planned to recruit subjects in Mexico was withdrawn as regulatory approval was not obtained), the actual number of subjects recruited in the study were therefore fewer than the planned number in

the protocol (314 actual versus 500 planned). However, there was no change in the power calculated to achieve the primary objective (as the required number of subjects were recruited). Appropriate changes were made to the Section 5.10.4, Determination of sample size, in the report.

6. STUDY POPULATION RESULTS

6.1. Study dates

The first subject was enrolled in the study on 23-October-2013 and the last study contact was on 03-July-2014. The data lock point (date of database freeze) occurred on 30-October 2014.

6.2. Subject disposition

The number of subjects who were vaccinated, completed or were withdrawn from the study, with reasons for withdrawal is presented in Table 18.

Table 18 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal for Month 6 (OTH=1) (Total vaccinated cohort)

	Q-QIV	TIV-YB	Total
Number of subjects vaccinated	158	156	314
Number of subjects completed	143	141	284
Number of subjects withdrawn	15	15	30
Reasons for withdrawal :			
Serious Adverse Event	0	0	0
Non-Serious Adverse Event	0	0	0
Protocol violation	1	0	1
Consent withdrawal (not due to an adverse event)	0	1	1
Migrated/moved from study area	0	0	0
Lost to follow-up (subjects with incomplete vaccination course)	3	5	8
Lost to follow-up (subjects with complete vaccination course)	1	1	2
Sponsor study termination	0	0	0
Others	1	0	1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come back for the last visit

The number of subjects enrolled in the study at each centre is presented in Table 41.

The number of subjects who received vaccination, completed or were withdrawn from the study at Day 28 and Day 56 and at Day 180 is presented in Table 42.

6.3. Important Protocol deviations at subject level

6.3.1. Protocol Deviations leading to elimination from ATP analyses

Table 19 presents the number of subjects excluded from ATP analysis.

Table 19 Number of subjects enrolled in the study and number of subjects excluded from ATP analyses

	Total			Q-QIV		TIV-YB		NOGRP	
Title	**n**	**s**	**%**	**n**	**s**	**n**	**s**	**n**	**s**
Total cohort	316			158		156		2	
Study vaccine dose not administrated but subject number allocated (code 1030)	2	2		0	0	0	0	2	2
Total vaccinated cohort	314		100	158		156		0	
Administration of vaccine(s) forbidden in the protocol (code 1040)	1	1		0	0	1	1	0	0
Randomisation failure (code 1050)	1	1		0	0	1	1	0	0
Others (reacto) (code 1500)	1	1		0	0	1	1	0	0
ATP cohort for safety	311		99.0	158		153		0	
Non compliance with vaccination schedule (including wrong and unknown dates) (code 2080)	2	2		0	0	2	2	0	0
Non compliance with blood sampling schedule (including wrong and unknown dates (code 2090)	4	4		2	2	2	2	0	0
Essential serological data missing (code 2100)	25	26		13	13	12	13	0	0
ATP cohort for immunogenicity	280		89.2	143		137		0	

NOGRP = No assigned group
Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
Note: Subjects may have more than one elimination code assigned
n = number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
s = number of subjects with the elimination code assigned
% = percentage of subjects in the considered ATP cohort relative to the Total vaccinated cohort
Others (Reacto) = Subject who had fever before the administration of Dose 2 (pre-vaccination temperature)

The deviations from specifications for age and intervals between study visits for primed and unprimed subjects are presented in Table 43 and Table 44, respectively.

6.3.2. Protocol Deviations not leading to elimination from ATP analyses

Two subjects' (No. (b) (6) were not observed for 30 minutes after vaccination (Dose 1) as the parents were unable to stay and had to leave. This was documented in the subjects' source.

6.4. Demographic characteristics and other baseline characteristics

The summary of demographic characteristics for TVC and ATP cohort for immunogenicity is presented in Table 20 and Table 21, respectively.

Table 20 Summary of demographic characteristics (Total vaccinated cohort)

		Q-QIV N = 158		TIV-YB N = 156		Total N = 314	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	19.6	-	19.8	-	19.7	-
	SD	8.8	-	8.9	-	8.9	-
	Median	20.5	-	21.0	-	21.0	-
	Minimum	6	-	6	-	6	-
	Maximum	35	-	35	-	35	-
Gender	Female	74	46.8	82	52.6	156	49.7
	Male	84	53.2	74	47.4	158	50.3
Ethnicity	American Hispanic or Latino	29	18.4	32	20.5	61	19.4
	Not American Hispanic or Latino	129	81.6	124	79.5	253	80.6
Geographic Ancestry	African Heritage / African American	56	35.4	56	35.9	112	35.7
	American Indian or Alaskan Native	1	0.6	0	0.0	1	0.3
	Asian - Central/South Asian Heritage	0	0.0	0	0.0	0	0.0
	Asian - East Asian Heritage	1	0.6	0	0.0	1	0.3
	Asian - Japanese Heritage	0	0.0	0	0.0	0	0.0
	Asian - South East Asian Heritage	0	0.0	1	0.6	1	0.3
	Native Hawaiian or Other Pacific Islander	0	0.0	0	0.0	0	0.0
	White - Arabic / North African Heritage	1	0.6	0	0.0	1	0.3
	White - Caucasian / European Heritage	86	54.4	88	56.4	174	55.4
	Other	13	8.2	11	7.1	24	7.6

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 21 Summary of demographic characteristics (ATP cohort for immunogenicity)

		Q-QIV N = 143		TIV-YB N = 137		Total N = 280	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	20.2	-	20.1	-	20.1	-
	SD	8.8	-	9.1	-	8.9	-
	Median	22.0	-	22.0	-	22.0	-
	Minimum	6	-	6	-	6	-
	Maximum	35	-	35	-	35	-
Gender	Female	67	46.9	71	51.8	138	49.3
	Male	76	53.1	66	48.2	142	50.7
Ethnicity	American Hispanic or Latino	27	18.9	29	21.2	56	20.0
	Not American Hispanic or Latino	116	81.1	108	78.8	224	80.0
Geographic Ancestry	African Heritage / African American	50	35.0	46	33.6	96	34.3
	American Indian or Alaskan Native	1	0.7	0	0.0	1	0.4
	Asian - Central/South Asian Heritage	0	0.0	0	0.0	0	0.0
	Asian - East Asian Heritage	1	0.7	0	0.0	1	0.4
	Asian - Japanese Heritage	0	0.0	0	0.0	0	0.0
	Asian - South East Asian Heritage	0	0.0	1	0.7	1	0.4
	Native Hawaiian or Other Pacific Islander	0	0.0	0	0.0	0	0.0
	White - Arabic / North African Heritage	1	0.7	0	0.0	1	0.4
	White - Caucasian / European Heritage	80	55.9	79	57.7	159	56.8
	Other	10	7.0	11	8.0	21	7.5

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

The age (in months) at vaccination Dose 1 by gender for the TVC and ATP cohort for immunogenicity, summary of vital characteristics at pre-vaccination, history of influenza vaccination in the previous 3 seasons and study population for the TVC is presented from Table 45 to Table 49.

The summary of demographic characteristics by age strata for the TVC and ATP cohort for immunogenicity is presented in Table 50 and Table 51, respectively.

The age (in months) at vaccination Dose 1 by gender and by age strata for the TVC and ATP cohort for immunogenicity, summary of vital characteristics at pre-vaccination, history of influenza vaccination in the previous 3 seasons and study population by age strata for the TVC is presented from Table 52 to Table 56.

The summary of demographic characteristics by priming status for the TVC and ATP cohort for immunogenicity is presented in Table 57 and Table 58, respectively.

The age (in months) at vaccination Dose 1 by gender and by priming status for the TVC and ATP cohort for immunogenicity, summary of vital characteristics at pre-vaccination, history of influenza vaccination in the previous 3 seasons and study population by priming status for the TVC is presented from Table 59 to Table 63.

7. IMMUNOGENICITY RESULTS

The analysis of immunogenicity was performed on the ATP cohort for immunogenicity (primary analysis). Since the percentage of subjects eliminated from the ATP cohort was more than 5%, a second (complementary) analysis was performed on the TVC.

7.1. According-to-protocol analysis

7.1.1. Primary immunogenicity objective

7.1.1.1. Seroconversion rate criterion

The results of the immunogenicity analysis of FLU Q-QIV based on CBER's SCR criterion for each of the four strains in children 6 to 35 months of age, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for primed and unprimed subjects, respectively) indicate that the criterion was met: the LLs of the two-sided 95% CI for SCR were greater than 40% (58.1% to 79.2%) (Table 22):

The SCR for HI antibodies against each strain was:

- 80.4% with a 95% CI [73.0%; 86.6%] for A/California/7/2009 (H1N1)
- 72.0% with a 95% CI [63.9%; 79.2%] or A/Texas/50/2012 (H3N2)
- 86.0% with a 95% CI [79.2%; 91.2%] for B/Massachusetts/2/2012 (Yamagata Lineage)
- 66.4% with a 95% CI [58.1%; 74.1%] for B/Brisbane/60/2008 (Victoria Lineage)

Table 22 Seroconversion rate (SCR) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for FLU Q-QIV and FLU TIV-YB (ATP cohort for immunogenicity)

			SCR			
					95% CI	
Antibody	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	143	115	80.4	73.0	86.6
	TIV-YB	137	98	71.5	63.2	78.9
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	143	103	72.0	63.9	79.2
	TIV-YB	137	94	68.6	60.1	76.3
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	143	123	86.0	79.2	91.2
	TIV-YB	137	115	83.9	76.7	89.7
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	143	95	66.4	58.1	74.1
	TIV-YB	137	17	12.4	7.4	19.1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as :
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

The SCR for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for FLU Q-QIV and FLU TIV-YB by age strata and priming status for the ATP cohort for immunogenicity is presented in Table 65 and Table 68, respectively.

7.1.2. Secondary immunogenicity objectives

7.1.2.1. Immunogenicity superiority of FLU-Q-QIV over *Fluzone* in terms of B/Victoria strain

The results indicate that the pre-defined statistical criteria required for demonstration of immunogenic superiority of FLU Q-QIV versus *Fluzone* in terms of GMT and SCR, in children 6 to 35 months of age, with respect to the B/Victoria strain present in FLU Q-QIV but absent in *Fluzone*, were met (superiority criteria: LL of the two-sided 95% CI of the adjusted GMT ratio > 1.5 *and* LL of the two-sided 95% CI for the SCR difference >10%).

For adjusted GMT ratios:

- The LL of the two-sided 95% CI for the GMT ratio of Q-QIV over *Fluzone* for the B/Brisbane/60/2008 strain (Victoria lineage) was 3.73, which was greater than 1.5.

For the SCR difference:

- The LL of the two-sided 95% CI for the SCR difference of Q-QIV minus *Fluzone* for the B/Brisbane/60/2008 (Victoria lineage) strain was 43.88%, which was greater than 10%.

Table 23 Adjusted GMT ratios of B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: Q-QIV/TIV-YB (ATP cohort for immunogenicity)

				Adjusted GMT ratio (Q-QIV / TIV-YB)		
Q-QIV		TIV-YB			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
143	64.7	137	13.7	4.73	3.73	5.99

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Analysis of co-variance (Ancova) model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 24 SCR Difference between groups for B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: Q-QIV minus TIV-YB (ATP cohort for immunogenicity)

							Difference in SCR (Q-QIV minus TIV-YB)		
	Q-QIV			TIV-YB				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	143	95	66.4	137	17	12.4	54.02	43.88	62.87

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as:
For initially seronegative subjects: post-vaccination antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

7.1.2.2. Immunogenicity of FLU Q-QIV and *Fluzone*

The seropositivity rates, seroprotection rates and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose for the ATP cohort for immunogenicity are presented in Table 25.

The MGI for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose for the ATP cohort for immunogenicity is presented in Table 26.

- At least 82.5% of subjects in the Q-QIV group and 80.3% of subjects in the TIV-YB group were seroprotected against the three strains, A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), 28 days after the last vaccination.
- In the Q-QIV group, 70.6% of subjects were seroprotected against the B/Brisbane/60/2008 (Victoria) strain, 28 days after the last vaccination.
- Q-QIV group has comparable or numerically higher GMT and MGI values at post-vaccination for all strains comparable to the TIV-YB groups.

Table 25 Seropositivity rates, seroprotection rates (SPR) and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose (ATP cohort for immunogenicity)

				≥ 10 1/DIL				≥ 40 1/DIL				GMT				
						95% CI				95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu A/California/7/2009 H1N1 HI	Q-QIV	PRE	143	56	39.2	31.1	47.7	25	17.5	11.6	24.7	10.3	8.6	12.3	<10.0	226.0
		POST	143	137	95.8	91.1	98.4	125	87.4	80.8	92.4	141.3	115.1	173.5	<10.0	1280.0
	TIV-YB	PRE	137	51	37.2	29.1	45.9	22	16.1	10.3	23.3	10.0	8.3	11.9	<10.0	226.0
		POST	137	130	94.9	89.8	97.9	111	81.0	73.4	87.2	90.8	73.2	112.6	<10.0	1280.0
Flu A/Texas/50/2012 H3N2 HI	Q-QIV	PRE	143	61	42.7	34.4	51.2	29	20.3	14.0	27.8	11.1	9.1	13.5	<10.0	453.0
		POST	143	141	98.6	95.0	99.8	118	82.5	75.3	88.4	100.6	82.6	122.6	<10.0	1280.0
	TIV-YB	PRE	137	58	42.3	33.9	51.1	25	18.2	12.2	25.7	11.5	9.3	14.2	<10.0	453.0
		POST	137	135	98.5	94.8	99.8	110	80.3	72.6	86.6	86.2	70.6	105.4	<10.0	1810.0
Flu B/Massachusetts/2/2012 Yamagata HI	Q-QIV	PRE	143	87	60.8	52.3	68.9	31	21.7	15.2	29.3	14.5	12.1	17.5	<10.0	320.0
		POST	143	142	99.3	96.2	100	135	94.4	89.3	97.6	212.0	174.6	257.3	<10.0	1810.0
	TIV-YB	PRE	137	75	54.7	46.0	63.3	22	16.1	10.3	23.3	12.3	10.3	14.7	<10.0	453.0
		POST	137	133	97.1	92.7	99.2	124	90.5	84.3	94.9	140.0	113.9	172.0	<10.0	2560.0
Flu B/Brisbane/60/2008 Victoria HI	Q-QIV	PRE	143	35	24.5	17.7	32.4	13	9.1	4.9	15.0	7.7	6.6	9.1	<10.0	640.0
		POST	143	135	94.4	89.3	97.6	101	70.6	62.4	77.9	69.0	54.9	86.6	<10.0	3620.0
	TIV-YB	PRE	137	25	18.2	12.2	25.7	9	6.6	3.0	12.1	6.6	5.9	7.5	<10.0	226.0
		POST	137	76	55.5	46.7	64.0	27	19.7	13.4	27.4	12.8	10.6	15.4	<10.0	640.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
seropositivity=HI antibody titre ≥ 10 1/DIL
seroprotection=HI antibody titre ≥ 40 1/DIL
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Table 26 Mean geometric increase (MGI) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose (ATP cohort for immunogenicity)

							MGI ratio			
									95% CI	
Antibody	Group	N	Time point description	MGI	Time point description	MGI	Ratio order	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	143	POST	141.3	PRE	10.3	POST / PRE	13.73	11.10	16.99
	TIV-YB	137	POST	90.8	PRE	10.0	POST / PRE	9.11	7.32	11.33
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	143	POST	100.6	PRE	11.1	POST / PRE	9.09	7.69	10.76
	TIV-YB	137	POST	86.2	PRE	11.5	POST / PRE	7.53	6.36	8.90
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	143	POST	212.0	PRE	14.5	POST / PRE	14.59	11.72	18.16
	TIV-YB	137	POST	140.0	PRE	12.3	POST / PRE	11.36	9.09	14.19
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	143	POST	69.0	PRE	7.7	POST / PRE	8.94	7.34	10.89
	TIV-YB	137	POST	12.8	PRE	6.6	POST / PRE	1.93	1.69	2.19

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
MGI = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Seropositivity rates, seroprotection rates (SPR) and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by age strata and priming status for ATP cohort for immunogenicity are presented in Table 64 and Table 67, respectively.

The MGI for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose by age strata and priming status for the ATP cohort for immunogenicity is presented in Table 66 and Table 69, respectively.

The reverse cumulative distribution curves of Flu A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata) and B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity) are presented from Figure 1 to Figure 4.

7.1.3. Tertiary immunogenicity objective

The adjusted GMT ratios and the SCR difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata) at 28 days after the last vaccine dose: TIV-YB/Q-QIV and TIV-YB minus Q-QIV (ATP cohort for immunogenicity) are presented in Table 27 and Table 28.

Table 27 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata) at 28 days after the last vaccine dose: TIV-YB/Q-QIV (ATP cohort for immunogenicity)

					Adjusted GMT ratio (TIV-YB / Q-QIV)		
	TIV-YB		Q-QIV			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	137	91.5	143	140.3	0.65	0.50	0.86
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	137	85.3	143	101.7	0.84	0.68	1.04
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	137	144.4	143	205.8	0.70	0.54	0.92

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 28 SCR difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata) at 28 days after the last vaccine dose: TIV-YB minus Q-QIV (ATP cohort for immunogenicity)

							Difference in SCR (TIV-YB minus Q-QIV)		
	TIV-YB			Q-QIV				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	137	98	71.5	143	115	80.4	-8.89	-18.89	1.14
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	137	94	68.6	143	103	72.0	-3.41	-14.11	7.29
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	137	115	83.9	143	123	86.0	-2.07	-10.67	6.41

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as:
For initially seronegative subjects: post-vaccination antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

7.2. Total vaccinated cohort analysis

Since the percentage of vaccinated subjects with serological results excluded from the ATP cohort for analysis of immunogenicity was more than 5% (10.8%, Refer to Table 19), a second analysis based on the TVC was performed to complement the ATP analysis.

The results in the TVC were comparable to the results in the ATP Immunogenicity cohort.

The immunogenicity tables for the TVC are presented in Table 70 to Table 76, and Figure 5 to Figure 8.

7.3. Immunogenicity summary

- The primary immunogenicity objective was met, as the LL of the two-sided 95% CI for SCR was > 40% against all four strains (range 58.1% to 79.2%), approximately 28 days after completion of dosing.
- The confirmatory secondary objective was also met. The immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of adjusted GMT ratios and SCR difference) was concluded, as the LL of the two-sided 95% CI of the adjusted GMT ratio (FLU Q-QIV/*Fluzone*), 3.73, was greater than 1.5, and the LL of the two-sided 95% CI for the SCR difference (FLU Q-QIV minus *Fluzone*), 43.88%, was greater than 10%.

8. SAFETY RESULTS

The analysis of safety was performed on the TVC (primary analysis).

Information regarding the number and percentage of subjects who received study vaccine per number of doses received is detailed in Table 29. Compliance in returning symptom sheets is presented in Table 77.

Table 29 Number and percentage of subjects who received study vaccine doses (Total vaccinated cohort)

	Q-QIV N = 158		TIV-YB N = 156	
Total number of doses received	**n**	**%**	**n**	**%**
1	64	40.5	64	41.0
2	94	59.5	92	59.0
Any	158	100	156	100

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = number of subjects in each group included in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose

8.1. Total vaccinated cohort analysis

8.1.1. Overall incidence of solicited adverse events

The overall incidence of solicited AEs are detailed in Table 30, Table 31 (grade 3), Table 32 (causal relationship to vaccination), Table 33 (grade 3 with causal relationship to vaccination).

- During the 7-day post-vaccination period, at least one solicited AE was reported for 62.3% and 59.5% of subjects in the Q-QIV and TIV-YB groups, respectively. At least one grade 3 solicited AE was reported for 11.9% and 7.4% of subjects in the Q-QIV and TIV-YB groups, respectively.

Table 30 Incidence and nature of adverse events (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	150	85	56.7	48.3	64.7	150	77	51.3	43.0	59.6	150	45	30.0	22.8	38.0
	TIV-YB	147	79	53.7	45.3	62.0	147	71	48.3	40.0	56.7	147	44	29.9	22.7	38.0
Dose 2	Q-QIV	89	43	48.3	37.6	59.2	89	36	40.4	30.2	51.4	89	21	23.6	15.2	33.8
	TIV-YB	89	37	41.6	31.2	52.5	89	34	38.2	28.1	49.1	89	11	12.4	6.3	21.0
Overall/dose	Q-QIV	239	128	53.6	47.0	60.0	239	113	47.3	40.8	53.8	239	66	27.6	22.0	33.7
	TIV-YB	236	116	49.2	42.6	55.7	236	105	44.5	38.0	51.1	236	55	23.3	18.1	29.2
Overall/subject	Q-QIV	151	94	62.3	54.0	70.0	151	87	57.6	49.3	65.6	151	50	33.1	25.7	41.2
	TIV-YB	148	88	59.5	51.1	67.4	148	79	53.4	45.0	61.6	148	48	32.4	25.0	40.6

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 31 Incidence and nature of grade 3 adverse events (solicited only) reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	150	13	8.7	4.7	14.4	150	12	8.0	4.2	13.6	150	3	2.0	0.4	5.7
	TIV-YB	147	9	6.1	2.8	11.3	147	8	5.4	2.4	10.4	147	1	0.7	0.0	3.7
Dose 2	Q-QIV	89	7	7.9	3.2	15.5	89	7	7.9	3.2	15.5	89	2	2.2	0.3	7.9
	TIV-YB	89	2	2.2	0.3	7.9	89	2	2.2	0.3	7.9	89	0	0.0	0.0	4.1
Overall/dose	Q-QIV	239	20	8.4	5.2	12.6	239	19	7.9	4.9	12.1	239	5	2.1	0.7	4.8
	TIV-YB	236	11	4.7	2.3	8.2	236	10	4.2	2.1	7.7	236	1	0.4	0.0	2.3
Overall/subject	Q-QIV	151	18	11.9	7.2	18.2	151	17	11.3	6.7	17.4	151	4	2.6	0.7	6.6
	TIV-YB	148	11	7.4	3.8	12.9	148	10	6.8	3.3	12.1	148	1	0.7	0.0	3.7

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 32 Incidence and nature of adverse events (solicited only) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	150	78	52.0	43.7	60.2	150	66	44.0	35.9	52.3	150	45	30.0	22.8	38.0
	TIV-YB	147	75	51.0	42.7	59.3	147	61	41.5	33.4	49.9	147	44	29.9	22.7	38.0
Dose 2	Q-QIV	89	38	42.7	32.3	53.6	89	29	32.6	23.0	43.3	89	21	23.6	15.2	33.8
	TIV-YB	89	32	36.0	26.1	46.8	89	28	31.5	22.0	42.2	89	11	12.4	6.3	21.0
Overall/dose	Q-QIV	239	116	48.5	42.0	55.1	239	95	39.7	33.5	46.3	239	66	27.6	22.0	33.7
	TIV-YB	236	107	45.3	38.9	51.9	236	89	37.7	31.5	44.2	236	55	23.3	18.1	29.2
Overall/subject	Q-QIV	151	87	57.6	49.3	65.6	151	76	50.3	42.1	58.6	151	50	33.1	25.7	41.2
	TIV-YB	148	84	56.8	48.4	64.9	148	71	48.0	39.7	56.3	148	48	32.4	25.0	40.6

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 33 Incidence and nature of grade 3 adverse events (solicited only) with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	150	13	8.7	4.7	14.4	150	12	8.0	4.2	13.6	150	3	2.0	0.4	5.7
	TIV-YB	147	7	4.8	1.9	9.6	147	6	4.1	1.5	8.7	147	1	0.7	0.0	3.7
Dose 2	Q-QIV	89	4	4.5	1.2	11.1	89	4	4.5	1.2	11.1	89	2	2.2	0.3	7.9
	TIV-YB	89	1	1.1	0.0	6.1	89	1	1.1	0.0	6.1	89	0	0.0	0.0	4.1
Overall/dose	Q-QIV	239	17	7.1	4.2	11.1	239	16	6.7	3.9	10.6	239	5	2.1	0.7	4.8
	TIV-YB	236	8	3.4	1.5	6.6	236	7	3.0	1.2	6.0	236	1	0.4	0.0	2.3
Overall/subject	Q-QIV	151	15	9.9	5.7	15.9	151	14	9.3	5.2	15.1	151	4	2.6	0.7	6.6
	TIV-YB	148	8	5.4	2.4	10.4	148	7	4.7	1.9	9.5	148	1	0.7	0.0	3.7

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

8.1.2. Solicited local adverse events

The incidence of solicited local AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall for the TVC is presented in Table 34.

The duration of the solicited local and general AEs during the 7-day follow-up period for the TVC is presented in Table 36.

- Overall, injection site pain was the most frequently reported solicited local AE (31.8% and 32.4% of subjects in the Q-QIV and TIV-YB groups, respectively). Grade 3 injection site pain was reported for 2.6% and 0.7% of subjects, respectively.
- After Dose 1, the incidence of injection site pain was 28.7% and 29.9% of subjects in the Q-QIV and TIV-YB groups, respectively. After Dose 2, the incidence of injection site pain was 23.6% and 12.4% of subjects, respectively.
- Redness at injection site was reported for 1.3% and 0.0% of subjects in the Q-QIV and TIV-YB group, respectively. Swelling at injection site was reported for 0.0% and 0.7% of subjects in the Q-QIV and TIV-YB group, respectively. There were no reports of grade 3 redness or swelling.
- The median duration of any solicited local adverse events was between 1.0-1.5 days (Table 36).

Table 34 Incidence of solicited local adverse events reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Q-QIV					TIV-YB				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Pain	All	150	43	28.7	21.6	36.6	147	44	29.9	22.7	38.0
	Grade 2 or 3	150	11	7.3	3.7	12.7	147	11	7.5	3.8	13.0
	Grade 3	150	3	2.0	0.4	5.7	147	1	0.7	0.0	3.7
	Medical advice	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
Redness (mm)	All	150	2	1.3	0.2	4.7	147	0	0.0	0.0	2.5
	>50	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
	>100	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
	Medical advice	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
Swelling (mm)	All	150	0	0.0	0.0	2.4	147	1	0.7	0.0	3.7
	>50	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
	>100	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
	Medical advice	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
Dose 2											
Pain	All	89	21	23.6	15.2	33.8	89	11	12.4	6.3	21.0
	Grade 2 or 3	89	2	2.2	0.3	7.9	89	1	1.1	0.0	6.1
	Grade 3	89	2	2.2	0.3	7.9	89	0	0.0	0.0	4.1
	Medical advice	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
Redness (mm)	All	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
	>50	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
	>100	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
	Medical advice	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
Swelling (mm)	All	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
	>50	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
	>100	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
	Medical advice	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
Overall/dose											
Pain	All	239	64	26.8	21.3	32.9	236	55	23.3	18.1	29.2
	Grade 2 or 3	239	13	5.4	2.9	9.1	236	12	5.1	2.7	8.7
	Grade 3	239	5	2.1	0.7	4.8	236	1	0.4	0.0	2.3
	Medical advice	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
Redness (mm)	All	239	2	0.8	0.1	3.0	236	0	0.0	0.0	1.6
	>50	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
	>100	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
	Medical advice	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
Swelling (mm)	All	239	0	0.0	0.0	1.5	236	1	0.4	0.0	2.3
	>50	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
	>100	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
	Medical advice	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
Overall/subject											
Pain	All	151	48	31.8	24.5	39.9	148	48	32.4	25.0	40.6
	Grade 2 or 3	151	11	7.3	3.7	12.7	148	11	7.4	3.8	12.9
	Grade 3	151	4	2.6	0.7	6.6	148	1	0.7	0.0	3.7
	Medical advice	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5
Redness (mm)	All	151	2	1.3	0.2	4.7	148	0	0.0	0.0	2.5
	>50	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5
	>100	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5
	Medical advice	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5

		Q-QIV					TIV-YB				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Swelling (mm)	All	151	0	0.0	0.0	2.4	148	1	0.7	0.0	3.7
	>50	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5
	>100	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5
	Medical advice	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

8.1.3. Solicited general adverse events

The incidence of solicited general AEs reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall for TVC is presented in Table 35.

- Overall, irritability/ fussiness was the most frequently reported solicited general AE (50.3% and 45.3% of subjects in the Q-QIV and TIV-YB groups, respectively) followed by drowsiness (39.7% and 37.8% of subjects, in the Q-QIV and TIV-YB groups, respectively) and loss of appetite (32.5% and 31.1% of subjects in the Q-QIV and TIV-YB groups, respectively).
- Grade 3 irritability/fussiness was reported for 8.6% and 4.1% of subjects, respectively. Grade 3 drowsiness was reported for 4.0% and 2.0% of subjects, respectively. Grade 3 loss of appetite was reported for 3.3% and 2.7% of subjects, respectively.
- During the 7-day (Day 0-6) follow-up, fever (≥38°C) was reported for 6.6% and 6.8% of subjects in the Q-QIV and TIV-YB groups, respectively. Grade 3 or higher fever (>39°C) was reported for 1.3% and 2.0% of subjects, respectively.
- Most of the solicited general AEs reported during the 7 days post-vaccination period were assessed by the investigator to be causally related to vaccination.
- The incidence of the solicited AEs was lower after Dose 2 in comparison to Dose 1. However, this difference was not statistically significant.
- The median duration of solicited general adverse events was between 1.0-2.0 days (Table 36).

Table 35 Incidence of solicited general adverse events reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Q-QIV					TIV-YB				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Drowsiness	All	150	56	37.3	29.6	45.6	147	48	32.7	25.2	40.9
	Grade 2 or 3	150	19	12.7	7.8	19.1	147	15	10.2	5.8	16.3
	Grade 3	150	4	2.7	0.7	6.7	147	2	1.4	0.2	4.8
	Related	150	47	31.3	24.0	39.4	147	41	27.9	20.8	35.9
	Grade 3 Related	150	4	2.7	0.7	6.7	147	1	0.7	0.0	3.7
	Medical advice	150	1	0.7	0.0	3.7	147	2	1.4	0.2	4.8
Fever/(Axillary) (°C)	All	150	7	4.7	1.9	9.4	147	8	5.4	2.4	10.4
	≥38	150	7	4.7	1.9	9.4	147	6	4.1	1.5	8.7
	>38.5	150	0	0.0	0.0	2.4	147	3	2.0	0.4	5.8
	>39.0	150	0	0.0	0.0	2.4	147	3	2.0	0.4	5.8
	>39.5	150	0	0.0	0.0	2.4	147	3	2.0	0.4	5.8
	>40.0	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
	Related	150	7	4.7	1.9	9.4	147	5	3.4	1.1	7.8
	≥38 Related	150	7	4.7	1.9	9.4	147	4	2.7	0.7	6.8
	>38.5 Related	150	0	0.0	0.0	2.4	147	2	1.4	0.2	4.8
	>39.0 Related	150	0	0.0	0.0	2.4	147	2	1.4	0.2	4.8
	>39.5 Related	150	0	0.0	0.0	2.4	147	2	1.4	0.2	4.8
	>40.0 Related	150	0	0.0	0.0	2.4	147	0	0.0	0.0	2.5
	Medical advice	150	0	0.0	0.0	2.4	147	3	2.0	0.4	5.8
Irritability / Fussiness	All	150	64	42.7	34.6	51.0	147	62	42.2	34.1	50.6
	Grade 2 or 3	150	24	16.0	10.5	22.9	147	23	15.6	10.2	22.5
	Grade 3	150	10	6.7	3.2	11.9	147	6	4.1	1.5	8.7
	Related	150	55	36.7	29.0	44.9	147	53	36.1	28.3	44.4
	Grade 3 Related	150	10	6.7	3.2	11.9	147	4	2.7	0.7	6.8
	Medical advice	150	1	0.7	0.0	3.7	147	4	2.7	0.7	6.8
Loss Of Appetite	All	150	41	27.3	20.4	35.2	147	40	27.2	20.2	35.2
	Grade 2 or 3	150	16	10.7	6.2	16.7	147	12	8.2	4.3	13.8
	Grade 3	150	3	2.0	0.4	5.7	147	3	2.0	0.4	5.8
	Related	150	39	26.0	19.2	33.8	147	34	23.1	16.6	30.8
	Grade 3 Related	150	3	2.0	0.4	5.7	147	1	0.7	0.0	3.7
	Medical advice	150	0	0.0	0.0	2.4	147	3	2.0	0.4	5.8
Dose 2											
Drowsiness	All	89	22	24.7	16.2	35.0	89	20	22.5	14.3	32.6
	Grade 2 or 3	89	5	5.6	1.8	12.6	89	6	6.7	2.5	14.1
	Grade 3	89	4	4.5	1.2	11.1	89	1	1.1	0.0	6.1
	Related	89	18	20.2	12.4	30.1	89	15	16.9	9.8	26.3
	Grade 3 Related	89	3	3.4	0.7	9.5	89	0	0.0	0.0	4.1
	Medical advice	89	2	2.2	0.3	7.9	89	0	0.0	0.0	4.1
Fever/(Axillary) (°C)	All	89	3	3.4	0.7	9.5	89	4	4.5	1.2	11.1
	≥38	89	3	3.4	0.7	9.5	89	4	4.5	1.2	11.1
	>38.5	89	2	2.2	0.3	7.9	89	0	0.0	0.0	4.1
	>39.0	89	2	2.2	0.3	7.9	89	0	0.0	0.0	4.1
	>39.5	89	2	2.2	0.3	7.9	89	0	0.0	0.0	4.1
	>40.0	89	1	1.1	0.0	6.1	89	0	0.0	0.0	4.1
	Related	89	2	2.2	0.3	7.9	89	4	4.5	1.2	11.1
	≥38 Related	89	2	2.2	0.3	7.9	89	4	4.5	1.2	11.1
	>38.5 Related	89	1	1.1	0.0	6.1	89	0	0.0	0.0	4.1
	>39.0 Related	89	1	1.1	0.0	6.1	89	0	0.0	0.0	4.1

		Q-QIV					TIV-YB				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Fever/(Axillary) (°C)	>39.5 Related	89	1	1.1	0.0	6.1	89	0	0.0	0.0	4.1
	>40.0 Related	89	0	0.0	0.0	4.1	89	0	0.0	0.0	4.1
	Medical advice	89	1	1.1	0.0	6.1	89	0	0.0	0.0	4.1
Irritability / Fussiness	All	89	34	38.2	28.1	49.1	89	27	30.3	21.0	41.0
	Grade 2 or 3	89	11	12.4	6.3	21.0	89	8	9.0	4.0	16.9
	Grade 3	89	4	4.5	1.2	11.1	89	0	0.0	0.0	4.1
	Related	89	26	29.2	20.1	39.8	89	22	24.7	16.2	35.0
	Grade 3 Related	89	3	3.4	0.7	9.5	89	0	0.0	0.0	4.1
	Medical advice	89	3	3.4	0.7	9.5	89	0	0.0	0.0	4.1
Loss Of Appetite	All	89	17	19.1	11.5	28.8	89	13	14.6	8.0	23.7
	Grade 2 or 3	89	8	9.0	4.0	16.9	89	5	5.6	1.8	12.6
	Grade 3	89	4	4.5	1.2	11.1	89	1	1.1	0.0	6.1
	Related	89	14	15.7	8.9	25.0	89	12	13.5	7.2	22.4
	Grade 3 Related	89	3	3.4	0.7	9.5	89	1	1.1	0.0	6.1
	Medical advice	89	3	3.4	0.7	9.5	89	0	0.0	0.0	4.1
Overall/dose											
Drowsiness	All	239	78	32.6	26.7	39.0	236	68	28.8	23.1	35.0
	Grade 2 or 3	239	24	10.0	6.5	14.6	236	21	8.9	5.6	13.3
	Grade 3	239	8	3.3	1.5	6.5	236	3	1.3	0.3	3.7
	Related	239	65	27.2	21.7	33.3	236	56	23.7	18.5	29.7
	Grade 3 Related	239	7	2.9	1.2	5.9	236	1	0.4	0.0	2.3
	Medical advice	239	3	1.3	0.3	3.6	236	2	0.8	0.1	3.0
Fever/(Axillary) (°C)	All	239	10	4.2	2.0	7.6	236	12	5.1	2.7	8.7
	≥38	239	10	4.2	2.0	7.6	236	10	4.2	2.1	7.7
	>38.5	239	2	0.8	0.1	3.0	236	3	1.3	0.3	3.7
	>39.0	239	2	0.8	0.1	3.0	236	3	1.3	0.3	3.7
	>39.5	239	2	0.8	0.1	3.0	236	3	1.3	0.3	3.7
	>40.0	239	1	0.4	0.0	2.3	236	0	0.0	0.0	1.6
	Related	239	9	3.8	1.7	7.0	236	9	3.8	1.8	7.1
	≥38 Related	239	9	3.8	1.7	7.0	236	8	3.4	1.5	6.6
	>38.5 Related	239	1	0.4	0.0	2.3	236	2	0.8	0.1	3.0
	>39.0 Related	239	1	0.4	0.0	2.3	236	2	0.8	0.1	3.0
	>39.5 Related	239	1	0.4	0.0	2.3	236	2	0.8	0.1	3.0
	>40.0 Related	239	0	0.0	0.0	1.5	236	0	0.0	0.0	1.6
	Medical advice	239	1	0.4	0.0	2.3	236	3	1.3	0.3	3.7
Irritability / Fussiness	All	239	98	41.0	34.7	47.5	236	89	37.7	31.5	44.2
	Grade 2 or 3	239	35	14.6	10.4	19.8	236	31	13.1	9.1	18.1
	Grade 3	239	14	5.9	3.2	9.6	236	6	2.5	0.9	5.5
	Related	239	81	33.9	27.9	40.3	236	75	31.8	25.9	38.1
	Grade 3 Related	239	13	5.4	2.9	9.1	236	4	1.7	0.5	4.3
	Medical advice	239	4	1.7	0.5	4.2	236	4	1.7	0.5	4.3
Loss Of Appetite	All	239	58	24.3	19.0	30.2	236	53	22.5	17.3	28.3
	Grade 2 or 3	239	24	10.0	6.5	14.6	236	17	7.2	4.3	11.3
	Grade 3	239	7	2.9	1.2	5.9	236	4	1.7	0.5	4.3
	Related	239	53	22.2	17.1	28.0	236	46	19.5	14.6	25.1
	Grade 3 Related	239	6	2.5	0.9	5.4	236	2	0.8	0.1	3.0
	Medical advice	239	3	1.3	0.3	3.6	236	3	1.3	0.3	3.7

		Q-QIV					TIV-YB				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject											
Drowsiness	All	151	60	39.7	31.9	48.0	148	56	37.8	30.0	46.2
	Grade 2 or 3	151	21	13.9	8.8	20.5	148	18	12.2	7.4	18.5
	Grade 3	151	6	4.0	1.5	8.4	148	3	2.0	0.4	5.8
	Related	151	52	34.4	26.9	42.6	148	48	32.4	25.0	40.6
	Grade 3 Related	151	5	3.3	1.1	7.6	148	1	0.7	0.0	3.7
	Medical advice	151	3	2.0	0.4	5.7	148	2	1.4	0.2	4.8
Fever/(Axillary) (°C)	All	151	10	6.6	3.2	11.8	148	11	7.4	3.8	12.9
	≥38	151	10	6.6	3.2	11.8	148	10	6.8	3.3	12.1
	>38.5	151	2	1.3	0.2	4.7	148	3	2.0	0.4	5.8
	>39.0	151	2	1.3	0.2	4.7	148	3	2.0	0.4	5.8
	>39.5	151	2	1.3	0.2	4.7	148	3	2.0	0.4	5.8
	>40.0	151	1	0.7	0.0	3.6	148	0	0.0	0.0	2.5
	Related	151	9	6.0	2.8	11.0	148	8	5.4	2.4	10.4
	≥38 Related	151	9	6.0	2.8	11.0	148	8	5.4	2.4	10.4
	>38.5 Related	151	1	0.7	0.0	3.6	148	2	1.4	0.2	4.8
	>39.0 Related	151	1	0.7	0.0	3.6	148	2	1.4	0.2	4.8
	>39.5 Related	151	1	0.7	0.0	3.6	148	2	1.4	0.2	4.8
	>40.0 Related	151	0	0.0	0.0	2.4	148	0	0.0	0.0	2.5
	Medical advice	151	1	0.7	0.0	3.6	148	3	2.0	0.4	5.8
Irritability / Fussiness	All	151	76	50.3	42.1	58.6	148	67	45.3	37.1	53.7
	Grade 2 or 3	151	30	19.9	13.8	27.1	148	28	18.9	13.0	26.2
	Grade 3	151	13	8.6	4.7	14.3	148	6	4.1	1.5	8.6
	Related	151	66	43.7	35.7	52.0	148	60	40.5	32.6	48.9
	Grade 3 Related	151	12	7.9	4.2	13.5	148	4	2.7	0.7	6.8
	Medical advice	151	4	2.6	0.7	6.6	148	4	2.7	0.7	6.8
Loss Of Appetite	All	151	49	32.5	25.1	40.5	148	46	31.1	23.7	39.2
	Grade 2 or 3	151	21	13.9	8.8	20.5	148	17	11.5	6.8	17.8
	Grade 3	151	5	3.3	1.1	7.6	148	4	2.7	0.7	6.8
	Related	151	46	30.5	23.2	38.5	148	39	26.4	19.5	34.2
	Grade 3 Related	151	4	2.6	0.7	6.6	148	2	1.4	0.2	4.8
	Medical advice	151	3	2.0	0.4	5.7	148	3	2.0	0.4	5.8

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 36 Number of days with solicited local and general adverse events during the 7-day follow-up period (Total vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max
Drowsiness	Dose 1	Q-QIV	56	1.9	1.0	1.0	1.0	2.0	7.0
		TIV-YB	48	2.1	1.0	1.0	2.0	2.0	7.0
	Dose 2	Q-QIV	22	2.4	1.0	1.0	2.0	3.0	6.0
		TIV-YB	20	2.2	1.0	1.0	1.0	2.5	7.0
	Overall/dose	Q-QIV	78	2.0	1.0	1.0	2.0	2.0	7.0
		TIV-YB	68	2.1	1.0	1.0	2.0	2.0	7.0
Irritability / fussiness	Dose 1	Q-QIV	64	2.6	1.0	1.0	2.0	3.5	7.0
		TIV-YB	62	2.4	1.0	1.0	2.0	3.0	6.0
	Dose 2	Q-QIV	34	2.1	1.0	1.0	1.0	3.0	6.0
		TIV-YB	27	2.3	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	98	2.4	1.0	1.0	2.0	3.0	7.0
		TIV-YB	89	2.4	1.0	1.0	2.0	3.0	7.0
Loss of appetite	Dose 1	Q-QIV	41	2.5	1.0	1.0	2.0	3.0	7.0
		TIV-YB	40	2.3	1.0	1.0	2.0	3.0	7.0
	Dose 2	Q-QIV	17	2.6	1.0	1.0	2.0	3.0	7.0
		TIV-YB	13	2.8	1.0	2.0	2.0	4.0	7.0
	Overall/dose	Q-QIV	58	2.5	1.0	1.0	2.0	3.0	7.0
		TIV-YB	53	2.4	1.0	1.0	2.0	3.0	7.0
Pain	Dose 1	Q-QIV	43	1.7	1.0	1.0	1.0	2.0	5.0
		TIV-YB	44	1.8	1.0	1.0	1.0	2.0	7.0
	Dose 2	Q-QIV	21	1.5	1.0	1.0	1.0	2.0	5.0
		TIV-YB	11	1.3	1.0	1.0	1.0	2.0	2.0
	Overall/dose	Q-QIV	64	1.7	1.0	1.0	1.0	2.0	5.0
		TIV-YB	55	1.7	1.0	1.0	1.0	2.0	7.0
Redness	Dose 1	Q-QIV	2	1.5	1.0	1.0	1.5	2.0	2.0
	Overall/dose	Q-QIV	2	1.5	1.0	1.0	1.5	2.0	2.0
Swelling	Dose 1	TIV-YB	1	1.0	1.0	1.0	1.0	1.0	1.0
	Overall/dose	TIV-YB	1	1.0	1.0	1.0	1.0	1.0	1.0
Fever	Dose 1	Q-QIV	7	2.6	1.0	1.0	1.0	6.0	6.0
		TIV-YB	8	2.0	1.0	1.0	1.0	3.0	5.0
	Dose 2	Q-QIV	3	2.3	2.0	2.0	2.0	3.0	3.0
		TIV-YB	4	1.8	1.0	1.0	1.5	2.5	3.0
	Overall/dose	Q-QIV	10	2.5	1.0	1.0	2.0	3.0	6.0
		TIV-YB	12	1.9	1.0	1.0	1.0	2.5	5.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = number of doses with the symptom
Q1 = 25th percentile
Q3 = 75th percentile

8.1.3.1. Relative risk of fever of FLU Q-QIV compared to *Fluzone* during a 4-day follow-up period

The relative risk in percentage of subjects reporting fever during the 4-day (Days 0-3) and 48 hours (Day 0-1) post-vaccination period following each dose for the TVC is presented in Table 37 and Table 38, respectively.

The relative risk of any fever (≥38°C) for the subjects in the Q-QIV group compared to the subjects in the TIV-YB group, during a 4-day follow-up period was 0.86 with a 95% CI of [0.33; 2.23] (p-value = 0.7969).

The relative risk of grade 3 or above fever (>39.0°C) for subjects in the Q-QIV group compared to the subjects in the TIV-YB group, during a 4-day follow-up period was 0.00 (grade 3 fever was reported for none of the subjects in the Q-QIV group, and for one subject in the TIV-YB group post-dose 1) with a 95% CI of [0.00; 3.76] (p-value = 0.4950).

Table 37 Relative risk in percentage of subjects reporting a specified solicited general adverse event (Fever) during the 4-day (Days 0-3) post-vaccination period following each dose (Total vaccinated cohort)

								Relative Risk (Q-QIV over TIV-YB)			
		Q-QIV			TIV-YB				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Fever/(Axillary) (°C)	All	150	6	4.0	147	5	3.4	1.18	0.39	3.57	1.0000
	≥38	150	6	4.0	147	4	2.7	1.47	0.45	4.78	0.7498
	>38.5	150	0	0.0	147	1	0.7	0.00	0.00	3.76	0.4949
	>39.0	150	0	0.0	147	1	0.7	0.00	0.00	3.76	0.4949
	>39.5	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>40.0	150	0	0.0	147	0	0.0	INF	0.00	INF	
	Related	150	6	4.0	147	3	2.0	1.96	0.55	7.07	0.5013
	≥38 Related	150	6	4.0	147	3	2.0	1.96	0.55	7.07	0.5013
	>38.5 Related	150	0	0.0	147	1	0.7	0.00	0.00	3.76	0.4949
	>39.0 Related	150	0	0.0	147	1	0.7	0.00	0.00	3.76	0.4949
	>39.5 Related	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>40.0 Related	150	0	0.0	147	0	0.0	INF	0.00	INF	
	Medical advice	150	0	0.0	147	2	1.4	0.00	0.00	1.87	0.2441
Dose 2											
Fever/(Axillary) (°C)	All	89	1	1.1	89	4	4.5	0.25	0.04	1.63	0.3679
	≥38	89	1	1.1	89	4	4.5	0.25	0.04	1.63	0.3679
	>38.5	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.0	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.5	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>40.0	89	0	0.0	89	0	0.0	INF	0.00	INF	
	Related	89	1	1.1	89	4	4.5	0.25	0.04	1.63	0.3679
	≥38 Related	89	1	1.1	89	4	4.5	0.25	0.04	1.63	0.3679
	>38.5 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.0 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.5 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>40.0 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	Medical advice	89	0	0.0	89	0	0.0	INF	0.00	INF	

								Relative Risk (Q-QIV over TIV-YB)			
		Q-QIV			TIV-YB				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Overall/dose											
Fever/(Axillary) (°C)	All	239	7	2.9	236	9	3.8	0.77	0.30	1.96	0.6212
	≥38	239	7	2.9	236	8	3.4	0.86	0.33	2.26	0.7994
	>38.5	239	0	0.0	236	1	0.4	0.00	0.00	3.79	0.4968
	>39.0	239	0	0.0	236	1	0.4	0.00	0.00	3.79	0.4968
	>39.5	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>40.0	239	0	0.0	236	0	0.0	INF	0.00	INF	
	Related	239	7	2.9	236	7	3.0	0.99	0.37	2.66	1.0000
	≥38 Related	239	7	2.9	236	7	3.0	0.99	0.37	2.66	1.0000
	>38.5 Related	239	0	0.0	236	1	0.4	0.00	0.00	3.79	0.4968
	>39.0 Related	239	0	0.0	236	1	0.4	0.00	0.00	3.79	0.4968
	>39.5 Related	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>40.0 Related	239	0	0.0	236	0	0.0	INF	0.00	INF	
	Medical advice	239	0	0.0	236	2	0.8	0.00	0.00	1.89	0.2463
Overall/subject											
Fever/(Axillary) (°C)	All	151	7	4.6	148	9	6.1	0.76	0.30	1.93	0.6165
	≥38	151	7	4.6	148	8	5.4	0.86	0.33	2.23	0.7969
	>38.5	151	0	0.0	148	1	0.7	0.00	0.00	3.76	0.4950
	>39.0	151	0	0.0	148	1	0.7	0.00	0.00	3.76	0.4950
	>39.5	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>40.0	151	0	0.0	148	0	0.0	INF	0.00	INF	
	Related	151	7	4.6	148	7	4.7	0.98	0.37	2.62	1.0000
	≥38 Related	151	7	4.6	148	7	4.7	0.98	0.37	2.62	1.0000
	>38.5 Related	151	0	0.0	148	1	0.7	0.00	0.00	3.76	0.4950
	>39.0 Related	151	0	0.0	148	1	0.7	0.00	0.00	3.76	0.4950
	>39.5 Related	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>40.0 Related	151	0	0.0	148	0	0.0	INF	0.00	INF	
	Medical advice	151	0	0.0	148	2	1.4	0.00	0.00	1.87	0.2442

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval, LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test
INF=infinity

Table 38 Relative risk in percentage of subjects reporting a specified solicited general adverse event (Fever) during the 48 hours (Days 0-1) post-vaccination period following each dose (Total vaccinated cohort)

								Relative Risk (Q-QIV over TIV-YB)			
		Q-QIV			TIV-YB				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Fever/(Axillary) (°C)	All	150	5	3.3	147	3	2.0	1.63	0.44	6.12	0.7229
	≥38	150	5	3.3	147	2	1.4	2.45	0.56	10.86	0.4477
	>38.5	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>39.0	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>39.5	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>40.0	150	0	0.0	147	0	0.0	INF	0.00	INF	
	Related	150	5	3.3	147	2	1.4	2.45	0.56	10.86	0.4477
	≥38 Related	150	5	3.3	147	2	1.4	2.45	0.56	10.86	0.4477
	>38.5 Related	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>39.0 Related	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>39.5 Related	150	0	0.0	147	0	0.0	INF	0.00	INF	
	>40.0 Related	150	0	0.0	147	0	0.0	INF	0.00	INF	
	Medical advice	150	0	0.0	147	1	0.7	0.00	0.00	3.76	0.4949
Dose 2											
Fever/(Axillary) (°C)	All	89	0	0.0	89	4	4.5	0.00	0.00	0.94	0.1208
	≥38	89	0	0.0	89	4	4.5	0.00	0.00	0.94	0.1208
	>38.5	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.0	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.5	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>40.0	89	0	0.0	89	0	0.0	INF	0.00	INF	
	Related	89	0	0.0	89	4	4.5	0.00	0.00	0.94	0.1208
	≥38 Related	89	0	0.0	89	4	4.5	0.00	0.00	0.94	0.1208
	>38.5 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.0 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>39.5 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	>40.0 Related	89	0	0.0	89	0	0.0	INF	0.00	INF	
	Medical advice	89	0	0.0	89	0	0.0	INF	0.00	INF	
Overall/dose											
Fever/(Axillary) (°C)	All	239	5	2.1	236	7	3.0	0.71	0.24	2.08	0.5741
	≥38	239	5	2.1	236	6	2.5	0.82	0.27	2.51	0.7706
	>38.5	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>39.0	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>39.5	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>40.0	239	0	0.0	236	0	0.0	INF	0.00	INF	
	Related	239	5	2.1	236	6	2.5	0.82	0.27	2.51	0.7706
	≥38 Related	239	5	2.1	236	6	2.5	0.82	0.27	2.51	0.7706
	>38.5 Related	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>39.0 Related	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>39.5 Related	239	0	0.0	236	0	0.0	INF	0.00	INF	
	>40.0 Related	239	0	0.0	236	0	0.0	INF	0.00	INF	
	Medical advice	239	0	0.0	236	1	0.4	0.00	0.00	3.79	0.4968

								Relative Risk (Q-QIV over TIV-YB)			
		Q-QIV			TIV-YB				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Overall/subject											
Fever/(Axillary) (°C)	All	151	5	3.3	148	7	4.7	0.70	0.24	2.05	0.5699
	≥38	151	5	3.3	148	6	4.1	0.82	0.27	2.47	0.7683
	>38.5	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>39.0	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>39.5	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>40.0	151	0	0.0	148	0	0.0	INF	0.00	INF	
	Related	151	5	3.3	148	6	4.1	0.82	0.27	2.47	0.7683
	≥38 Related	151	5	3.3	148	6	4.1	0.82	0.27	2.47	0.7683
	>38.5 Related	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>39.0 Related	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>39.5 Related	151	0	0.0	148	0	0.0	INF	0.00	INF	
	>40.0 Related	151	0	0.0	148	0	0.0	INF	0.00	INF	
	Medical advice	151	0	0.0	148	1	0.7	0.00	0.00	3.76	0.4950

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = Standardized asymptotic 95% confidence interval, LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Fisher Exact Test
INF=infinity

8.1.4. Unsolicited adverse events

The percentage of subjects reporting the occurrence of unsolicited AEs, grade 3 unsolicited AEs, AEs with causal relationship to vaccination and grade 3 AEs with causal relationship to vaccination within the 28-day (Days 0-27) post-vaccination period for TVC is presented in Table 78, Table 80, Table 82 and Table 84, respectively.

The percentage of doses reporting the occurrence of unsolicited AEs, grade 3 unsolicited AEs, AEs with causal relationship to vaccination and grade 3 AEs with causal relationship to vaccination within the 28-day (Days 0-27) post-vaccination period for TVC is presented in Table 79, Table 81, Table 83 and Table 85, respectively.

- During the 28-day post-vaccination period, at least one unsolicited AE was reported for 48.7% and 48.1% of subjects in the Q-QIV and TIV-YB groups, respectively. Diarrhoea (9.5% of subjects) was the most frequently reported AE in the Q-QIV group, followed by cough (8.9% of subjects), rhinorrhoea (8.2% of subjects) and upper respiratory tract infection and otitis media (both in 7.0% of subjects). In the TIV-YB group, cough (8.3% of subjects) was the most frequently reported AE followed by rhinorrhoea, otitis media (both in 7.7% of subjects) and upper respiratory tract infection (7.1%).

- At least one grade 3 unsolicited AE was reported for 7.6% and 7.7% subjects in the Q-QIV and TIV-YB groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 7.0% and 4.5 % of subjects, respectively. At least one grade 3 unsolicited AE with causal relationship to vaccination was reported for 2 (1.3%) and 1 (0.6%) of subject(s), respectively.

8.1.4.1. Medically attended events

The percentage of subjects reporting the occurrence of unsolicited AEs with MAEs during the entire study period for the TVC is presented in Table 39.

- At least one unsolicited AE with a medically attended visit during the entire study period was reported for 48.7% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively.
- Otitis media was the most frequently reported MAE in both groups (14.6% and 19.2% of subjects, respectively) followed by upper respiratory tract infection (11.4% and 15.4% of subjects, respectively).

Table 39 Percentage of subjects reporting the occurrence of unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit (MAEs) during the entire study period (Total vaccinated cohort)

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		77	48.7	40.7	56.8	89	57.1	48.9	64.9
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Eosinophilia (10014950)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Lymphadenitis (10025188)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Lymphadenopathy (10025197)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Cardiac disorders (10007541)	Cyanosis (10011703)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Congenital, familial and genetic disorders (10010331)	Tibial torsion (10064515)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	2	1.3	0.2	4.5	1	0.6	0.0	3.5
	Conductive deafness (10010280)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Ear pain (10014020)	3	1.9	0.4	5.4	4	2.6	0.7	6.4
	Hyperacusis (10020559)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Tympanic membrane perforation (10045210)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Eye disorders (10015919)	Amblyopia (10001906)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Conjunctival haemorrhage (10010719)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Conjunctivitis allergic (10010744)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Ocular hyperaemia (10030041)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Strabismus (10042159)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Gastrointestinal disorders (10017947)	Constipation (10010774)	2	1.3	0.2	4.5	6	3.8	1.4	8.2
	Dental caries (10012318)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Diarrhoea (10012735)	3	1.9	0.4	5.4	4	2.6	0.7	6.4
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Nausea (10028813)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Teething (10043183)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Vomiting (10047700)	4	2.5	0.7	6.4	7	4.5	1.8	9.0
General disorders and administration site conditions (10018065)	Developmental delay (10012559)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Injection site bruising (10022052)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Pyrexia (10037660)	4	2.5	0.7	6.4	5	3.2	1.0	7.3
Immune system disorders (10021428)	Allergy to arthropod bite (10058285)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Drug hypersensitivity (10013700)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Milk allergy (10027633)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Seasonal allergy (10048908)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Infections and infestations (10021881)	Abscess neck (10053576)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Acrodermatitis (10063409)	2	1.3	0.2	4.5	0	0.0	0.0	2.3
	Acute sinusitis (10001076)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Adenovirus infection (10060931)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Bronchiolitis (10006448)	4	2.5	0.7	6.4	2	1.3	0.2	4.6
	Bronchitis (10006451)	3	1.9	0.4	5.4	1	0.6	0.0	3.5
	Candida infection (10074170)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Candida nappy rash (10007135)	2	1.3	0.2	4.5	5	3.2	1.0	7.3
	Carbuncle (10007247)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Cellulitis (10007882)	1	0.6	0.0	3.5	0	0.0	0.0	2.3

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Infections and infestations (10021881)	Conjunctivitis (10010741)	4	2.5	0.7	6.4	9	5.8	2.7	10.7
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Conjunctivitis viral (10010755)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Coxsackie viral infection (10011261)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Croup infectious (10011416)	3	1.9	0.4	5.4	1	0.6	0.0	3.5
	Ear infection (10014011)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Eczema infected (10014199)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	External ear cellulitis (10015729)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Folliculitis (10016936)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Furuncle (10017553)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Gastritis viral (10051791)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Gastroenteritis (10017888)	2	1.3	0.2	4.5	7	4.5	1.8	9.0
	Gastroenteritis viral (10017918)	2	1.3	0.2	4.5	3	1.9	0.4	5.5
	Genital candidiasis (10018143)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	H1n1 influenza (10069767)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Influenza (10022000)	1	0.6	0.0	3.5	3	1.9	0.4	5.5
	Localised infection (10024774)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Nasopharyngitis (10028810)	3	1.9	0.4	5.4	5	3.2	1.0	7.3
	Neonatal candida infection (10028924)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Onychomycosis (10030338)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Oral candidiasis (10030963)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Otitis media (10033078)	23	14.6	9.5	21.0	30	19.2	13.4	26.3
	Otitis media acute (10033079)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Otitis media chronic (10033081)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Paronychia (10034016)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Pharyngitis (10034835)	2	1.3	0.2	4.5	6	3.8	1.4	8.2
	Pharyngitis streptococcal (10034839)	1	0.6	0.0	3.5	3	1.9	0.4	5.5
	Pharyngotonsillitis (10049140)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Pneumonia (10035664)	0	0.0	0.0	2.3	4	2.6	0.7	6.4
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Respiratory syncytial virus infection (10061603)	4	2.5	0.7	6.4	3	1.9	0.4	5.5
	Respiratory tract infection (10062352)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Rhinitis (10039083)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Sinusitis (10040753)	2	1.3	0.2	4.5	6	3.8	1.4	8.2
	Staphylococcal abscess (10041917)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Tinea capitis (10043866)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Tinea faciei (10067719)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Tinea infection (10060889)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Tonsillitis (10044008)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Tracheobronchitis (10044314)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Upper respiratory tract infection (10046306)	18	11.4	6.9	17.4	24	15.4	10.1	22.0
	Urinary tract infection (10046571)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Urogenital infection fungal (10065582)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Viral infection (10047461)	12	7.6	4.0	12.9	12	7.7	4.0	13.1
	Viral rash (10047476)	0	0.0	0.0	2.3	6	3.8	1.4	8.2

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Infections and infestations (10021881)	Viral upper respiratory tract infection (10047482)	4	2.5	0.7	6.4	7	4.5	1.8	9.0
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Animal bite (10002515)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Arthropod bite (10003399)	1	0.6	0.0	3.5	4	2.6	0.7	6.4
	Burns first degree (10006797)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Burns second degree (10006802)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Contusion (10050584)	1	0.6	0.0	3.5	2	1.3	0.2	4.6
	Ear injury (10057446)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Exposure to toxic agent (10053487)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Foreign body (10070245)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Head injury (10019196)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Humerus fracture (10020462)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Joint injury (10060820)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Laceration (10023572)	4	2.5	0.7	6.4	1	0.6	0.0	3.5
	Ligament sprain (10024453)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Wound (10052428)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Wrist fracture (10048049)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Investigations (10022891)	Cardiac murmur (10007586)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Failure to thrive (10016165)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Hypercarotinaemia (10020594)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Lactose intolerance (10023681)	1	0.6	0.0	3.5	2	1.3	0.2	4.6
	Overweight (10033307)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Musculoskeletal and connective tissue disorders (10028395)	Ligament laxity (10024452)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Neck pain (10028836)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Pain in extremity (10033425)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
Nervous system disorders (10029205)	Convulsion (10010904)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Dizziness (10013573)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Gross motor delay (10069118)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Language disorder (10074869)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Speech disorder developmental (10041467)	0	0.0	0.0	2.3	4	2.6	0.7	6.4
Psychiatric disorders (10037175)	Abnormal behaviour (10061422)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Anxiety (10002855)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Autism spectrum disorder (10063844)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Insomnia (10022437)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Tic (10043833)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Renal and urinary disorders (10038359)	Dysuria (10013990)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Pollakiuria (10036018)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Reproductive system and breast disorders (10038604)	Testicular retraction (10043348)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	2	1.3	0.2	4.5	3	1.9	0.4	5.5
	Bronchial hyperreactivity (10066091)	1	0.6	0.0	3.5	3	1.9	0.4	5.5
	Bronchospasm (10006482)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Cough (10011224)	2	1.3	0.2	4.5	3	1.9	0.4	5.5
	Nasal congestion (10028735)	2	1.3	0.2	4.5	1	0.6	0.0	3.5

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Respiratory, thoracic and mediastinal disorders (10038738)	Rhinitis allergic (10039085)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Rhinorrhoea (10039101)	1	0.6	0.0	3.5	2	1.3	0.2	4.6
	Sleep apnoea syndrome (10040979)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Wheezing (10047924)	1	0.6	0.0	3.5	2	1.3	0.2	4.6
Skin and subcutaneous tissue disorders (10040785)	Dermatitis (10012431)	2	1.3	0.2	4.5	0	0.0	0.0	2.3
	Dermatitis atopic (10012438)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Dermatitis contact (10012442)	2	1.3	0.2	4.5	4	2.6	0.7	6.4
	Dermatitis diaper (10012444)	4	2.5	0.7	6.4	4	2.6	0.7	6.4
	Dry skin (10013786)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Eczema (10014184)	3	1.9	0.4	5.4	3	1.9	0.4	5.5
	Eczema nummular (10014201)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Hyperkeratosis (10020649)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Petechiae (10034754)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Rash (10037844)	2	1.3	0.2	4.5	1	0.6	0.0	3.5
	Skin lesion (10040882)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Social circumstances (10041244)	Overfeeding of infant (10059260)	0	0.0	0.0	2.3	1	0.6	0.0	3.5

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

8.2. According-to-protocol cohort analysis

The primary analysis of safety was performed on the TVC. Since the percentage of enrolled subjects excluded from the TVC for analysis of safety was less than 5%, no secondary analysis on the ATP cohort for safety was performed.

8.3. Serious adverse events

There were 5 (3.2%) subjects reporting 5 SAEs in the Q-QIV group and 4 (2.6%) subjects reporting 4 SAEs in the TIV-YB (*Fluzone*) group.

The serious adverse event (SAE) Listing Table(s) are in Section 13.1 (Table 91) and the Clinical Narratives for SAEs reports are in Section 13.2.

The percentage of subjects reporting the occurrence of SAEs during the entire study period for the TVC is presented in Table 40.

8.3.1. Fatal events

No fatal events were reported during the entire study period.

8.3.2. Non-fatal events

A total of 9 non-fatal SAEs were reported for 9 subjects [5 (3.2%) subjects in the Q-QIV group and 4 (2.6%) subjects in the TIV-YB group] during the entire study period. All events except 2 (sleep apnoea syndrome and convulsion) were considered recovered or resolved at the time of this report. None of these events was considered related to the study vaccine in the opinion of the investigator.

Table 40 Percentage of subjects reporting the occurrence of serious adverse events (SAEs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire study period (Total vaccinated cohort)

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		5	3.2	1.0	7.2	4	2.6	0.7	6.4
Infections and infestations (10021881)	Abscess neck (10053576)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Respiratory syncytial virus infection (10061603)	2	1.3	0.2	4.5	0	0.0	0.0	2.3
	Viral infection (10047461)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Failure to thrive (10016165)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Nervous system disorders (10029205)	Convulsion (10010904)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Respiratory, thoracic and mediastinal disorders (10038738)	Sleep apnoea syndrome (10040979)	1	0.6	0.0	3.5	0	0.0	0.0	2.3

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

8.4. Adverse events leading to premature discontinuation of study vaccine and/or study

No AEs or SAEs leading to premature discontinuation of study vaccine were reported in this study.

8.5. Other significant adverse events

8.5.1. Potential immune-mediated diseases

No pIMDs were reported during the entire study period.

8.6. Concomitant medications /vaccinations

The results regarding concomitant medications and vaccinations are detailed in Table 86, Table 87, Table 88, Table 89 and Table 90.

During the entire study period:

- Any concomitant medications were used by 51.3% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively.
- Any antipyretic was taken by 32.9% and 39.1% of subjects, respectively. Antipyretics were taken prophylactically in anticipation of reaction to vaccination by 4.4% and 3.8% of subjects, respectively.
- Any antibiotic was taken by 22.2% and 29.5% of subjects, respectively. None of them were taken prophylactically.
- The most frequently administered concomitant vaccinations on the same day as study vaccination were Hepatitis A vaccine (received by 13.9% and 10.9% of subjects in the Q-QIV and TIV-YB groups, respectively) followed by pneumocaccal conjugate vaccine (received by 13.9% and 12.2% of subjects, respectively) and *Haemophilus influenzae* type b vaccine (received by 12.0% and 10.3% of subjects, respectively).

8.7. Safety summary

A descriptive summary of safety data is provided in this section. These data, together with the safety data from other studies will contribute to the safety evaluation of the product.

- *Solicited local AEs*: Overall, injection site pain was the most frequently reported solicited local AE (31.8% and 32.4% of subjects in the Q-QIV and TIV-YB groups, respectively). Grade 3 injection site pain was reported for 2.6% and 0.7% of subjects, respectively.
- *Solicited general AEs*: Overall, irritability/fussiness was the most frequently reported solicited general AE (50.3% and 45.3% of subjects in the Q-QIV and TIV-YB groups, respectively). Grade 3 irritability/fussiness was reported for 8.6% and 4.1% of subjects, respectively. Fever (≥38°C) was reported for 6.6% and 6.8% of subjects in the Q-QIV and TIV-YB groups, respectively. Grade 3 or higher fever (>39.0°C) was reported for 1.3% and 2.0% of subjects, respectively.
- *Relative risk of fever:* The relative risk of any fever (≥38°C) for Q-QIV compared to TIV-YB during a 4-day follow-up period was 0.86 with a 95% CI of [0.33; 2.23] (p-value = 0.7969). The relative risk of grade 3 or above fever (>39.0°C) for Q-QIV compared to TIV-YB during a 4-day follow-up period was 0.00 (grade 3 fever was reported for none of the subjects in the Q-QIV group, and for one subject in the TIV-YB group post-dose 1) with a 95% CI of [0.00; 3.76] (p-value = 0.4950).
- *Unsolicited AEs*: During the 28-day post-vaccination period, at least one unsolicited AE was reported for 48.7% and 48.1% of subjects in the Q-QIV and TIV-YB groups, respectively. Diarrhoea (9.5% of subjects) was the most frequently reported AE in

the Q-QIV group while in the TIV-YB group, cough (8.3% of subjects) was the most frequently reported AE. At least one grade 3 unsolicited AE was reported for 7.6% and 7.7% subjects in the Q-QIV and TIV-YB groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 7.0% and 4.5 % of subjects, respectively. At least one grade 3 unsolicited AE with causal relationship to vaccination was reported for 2 (1.3%) and 1 (0.6%) of subject(s), respectively.

- *MAEs*: At least one unsolicited AE with a medically attended visit during the entire study period was reported for 48.7% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively. Otitis media was the most frequently reported MAE in both groups (14.6% and 19.2% of subjects, respectively).
- *pIMDs*: No pIMDs were reported in the study.
- *SAEs*: A total of 9 non-fatal SAEs were reported for 9 subjects [5 (3.2%) subjects in the Q-QIV group and 4 (2.6%) subjects in the TIV-YB group] during the entire study period. All events except 2 (sleep apnoea syndrome and convulsion) were considered recovered or resolved at the time of this report. None of these events was considered related to the study vaccine in the opinion of the investigator. No fatal SAEs were reported.
- *Concomitant medication*: Any concomitant medications were used by 51.3% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively, during the entire study period.

9. OVERALL CONCLUSIONS

- The primary immunogenicity objective was met, since the LL of the two-sided 95% CI for SCR was >40% against all four strains (range 58.1% to 79.2%), approximately 28 days after completion of dosing.
- The confirmatory secondary objective of demonstrating the immunogenic superiority of the B/Victoria strain present in FLU Q-QIV (in terms of adjusted GMT ratios and SCR difference) was also met, since the LL of the two-sided 95% CI of the adjusted GMT ratio (FLU Q-QIV/*Fluzone*), 3.73, was greater than 1.5, and the LL of the two-sided 95% CI for the SCR difference (FLU Q-QIV minus *Fluzone*), 43.88% was greater than 10%.
- During the 28-day post-vaccination period, at least one unsolicited AE was reported for 48.7% and 48.1% of subjects in the Q-QIV and TIV-YB groups, respectively. At least one grade 3 unsolicited AE was reported for 7.6% and 7.7% subjects in the Q-QIV and TIV-YB groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 7.0% and 4.5 % of subjects, respectively.
- At least one unsolicited AE with a medically attended visit during the entire study period was reported for 48.7% and 57.1% of subjects in the Q-QIV and TIV-YB groups, respectively. Otitis media was the most frequently reported MAE in both groups (14.6% and 19.2% of subjects, respectively).
- A total of 9 non-fatal SAEs were reported for 9 subjects [5 (3.2%) subjects in the Q-QIV group and 4 (2.6%) subjects in the TIV-YB group] during the entire study period. All events except 2 (sleep apnoea syndrome and convulsion) were considered recovered or resolved at the time of this report. None of these events was considered related to the study vaccine in the opinion of the investigator. No fatal SAEs were reported.
- No other safety concerns were identified. The FLU Q-QIV and *Fluzone* vaccines were generally well tolerated.

10. POST-TEXT TABLES AND FIGURES

10.1. Study Population

Table 41 Number of subjects by center (Total vaccinated cohort)

	Q-QIV	TIV-YB	Total	
Center	**n**	**n**	**n**	**%**
204456	38	37	75	23.9
204457	16	13	29	9.2
204459	9	9	18	5.7
204460	3	5	8	2.5
204462	12	11	23	7.3
204463	12	14	26	8.3
204464	15	15	30	9.6
204614	4	4	8	2.5
204615	13	12	25	8.0
204616	9	8	17	5.4
204618	6	7	13	4.1
204690	21	21	42	13.4
All	158	156	314	100

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
n = number of subjects included in each group or in total for a given center or for all centers
All = sum of all subjects in each group or in total (sum of all groups)
% = n/All x 100
Center = GSK Biologicals assigned center number

Table 42 Number of subjects at each visit and list of withdrawn subjects (Total vaccinated cohort)

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
Q-QIV	VISIT 1 - D0	158		
			(b) (6)	Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Protocol violation
	VISIT 2 - D28	154		
				Lost to follow-up
				Missed visit
	VISIT 3 - D56	95		
	TC - D180	143		
TIV-YB	VISIT 1 - D0	156		
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
	VISIT 2 - D28	150		
				Lost to follow-up
	VISIT 3 - D56	92		
	TC - D180	141		
Total	VISIT 1 - D0	314		
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Protocol violation
				Lost to follow-up
				Lost to follow-up

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
	VISIT 2 - D28	304		
			(b) (6)	
				Lost to follow-up
				Missed visit
				Lost to follow-up
	VISIT 3 - D56	187		
	TC - D180	284		

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

Table 43 Deviations from specifications for age and intervals between study visits for primed subjects (Total vaccinated cohort)

		Age	Dose:1-PI(D28)	Dose:1-TC - D180
Group		**Protocol**	**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days	from 166 to 201 days
Q-QIV	N	57	56	54
	n	0	0	1
	%	0.0	0.0	1.9
	range	15 to 35	25 to 42	166 to 210
TIV-YB	N	57	54	53
	n	0	0	0
	%	0.0	0.0	0.0
	range	15 to 35	25 to 42	166 to 201

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Table 44 Deviations from specifications for age and intervals between study visits for unprimed subjects (Total vaccinated cohort)

		Age	Dose:1-Dose:2	Dose:2-PII(D56)	Dose:1-TC - D180
Group		**Protocol**	**Protocol**	**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days	from 25 to 42 days	from 166 to 201 days
Q-QIV	N	101	94	89	89
	n	0	0	2	0
	%	0.0	0.0	2.2	0.0
	range	6 to 35	25 to 42	22 to 44	166 to 201
TIV-YB	N	99	92	89	88
	n	0	2	2	0
	%	0.0	2.2	2.2	0.0
	range	6 to 34	25 to 57	22 to 42	166 to 201

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Table 45 Age (in months) at vaccination Dose 1 by gender (Total vaccinated cohort)

Group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	F	74	74	20.7	8.4	6	35
	M	84	84	18.7	9.2	6	35
	Total	158	158	19.6	8.8	6	35
TIV-YB	F	82	82	20.1	8.5	6	35
	M	74	74	19.5	9.4	6	35
	Total	156	156	19.8	8.9	6	35
ALL	F	156	156	20.4	8.4	6	35
	M	158	158	19.0	9.3	6	35
	Total	314	314	19.7	8.9	6	35

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 46 Age (in months) at vaccination Dose 1 by gender (ATP cohort for immunogenicity)

Group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	F	67	67	21.5	8.1	6	35
	M	76	76	19.0	9.3	6	35
	Total	143	143	20.2	8.8	6	35
TIV-YB	F	71	71	20.4	8.6	6	35
	M	66	66	19.7	9.6	6	35
	Total	137	137	20.1	9.1	6	35
ALL	F	138	138	21.0	8.4	6	35
	M	142	142	19.3	9.4	6	35
	Total	280	280	20.1	8.9	6	35

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 47 Summary of vital signs characteristics at pre-vaccination (Total vaccinated cohort)

		Q-QIV (N = 158)	TIV-YB (N = 156)	Total (N = 314)
Characteristics	Parameters	Value	Value	Value
Height (cm)	Mean	82.1	82.2	82.2
	SD	9.3	9.5	9.4
	Median	84.0	84.0	84.0
	Minimum	64.0	63.0	63.0
	Maximum	102.0	107.0	107.0
	Unknown	1	0	1
Weight (kg)	Mean	11.9	11.8	11.8
	SD	3.6	3.3	3.4
	Median	11.4	11.6	11.5
	Minimum	7.0	6.7	6.7
	Maximum	35.0	34.0	35.0
	Unknown	1	0	1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 48 History of influenza vaccination in the previous 3 seasons (Total vaccinated cohort)

		Q-QIV N = 158		TIV-YB N = 156		Total N = 314	
Characteristics	**Parameters or Categories**	**n**	**%**	**n**	**%**	**n**	**%**
At least one season	Yes	74	46.8	72	46.2	146	46.5
	No	84	53.2	84	53.8	168	53.5
Season 2013-2012	Yes	66	41.8	61	39.1	127	40.4
Season 2012-2011	Yes	24	15.2	35	22.4	59	18.8
Season 2011-2010	Yes	1	0.6	3	1.9	4	1.3

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N=Total number of subjects
n=number of subjects with influenza vaccination during the specified season
%=n / Number of subjects with available results * 100

Table 49 Study population (Total vaccinated cohort)

Number of subjects	**Q-QIV**	**TIV-YB**	**Total**
Planned, N	250	250	500
Randomised, N (Total Vaccinated Cohort)	158	156	314
Completed Month 6 visit, n (%)	143 (90.5)	141 (90.4)	284 (90.4)
Demographics	Q-QIV	TIV-YB	Total
N (Total Vaccinated Cohort)	158	156	314
Females:Males	74:84	82:74	156:158
Mean Age, months (SD)	19.6 (8.8)	19.8 (8.9)	19.7 (8.9)
Median Age, months (minimum, maximum)	21 (6, 35)	21 (6, 35)	21 (6, 35)
White - Caucasian / European Heritage, n (%)	86 (54.4)	88 (56.4)	174 (55.4)
African Heritage / African American, n (%)	56 (35.4)	56 (35.9)	112 (35.7)
Others, n (%)	13 (8.2)	11 (7.1)	24 (7.6)

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
N=total number of subjects
n/%=number/percentage of subjects
SD=standard deviation

Table 50 Summary of demographic characteristics by age strata (Total vaccinated cohort)

		Q-QIV				TIV-YB				Total			
		6-17M N = 64		18-35M N = 94		6-17M N = 62		18-35M N = 94		6-17M N = 126		18-35M N = 188	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	10.3	-	26.0	-	10.2	-	26.1	-	10.3	-	26.0	-
	SD	3.5	-	4.9	-	3.4	-	4.8	-	3.4	-	4.8	-
	Median	10.5	-	25.0	-	10.0	-	26.0	-	10.0	-	25.0	-
	Minimum	6	-	18	-	6	-	18	-	6	-	18	-
	Maximum	17	-	35	-	17	-	35	-	17	-	35	-
Gender	Female	28	43.8	46	48.9	34	54.8	48	51.1	62	49.2	94	50.0
	Male	36	56.3	48	51.1	28	45.2	46	48.9	64	50.8	94	50.0
Ethnicity	American Hispanic or Latino	14	21.9	15	16.0	14	22.6	18	19.1	28	22.2	33	17.6
	Not American Hispanic or Latino	50	78.1	79	84.0	48	77.4	76	80.9	98	77.8	155	82.4
Geographic Ancestry	African Heritage / African American	23	35.9	33	35.1	25	40.3	31	33.0	48	38.1	64	34.0
	American Indian or Alaskan Native	0	0.0	1	1.1	0	0.0	0	0.0	0	0.0	1	0.5
	Asian - Central/South Asian Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - East Asian Heritage	0	0.0	1	1.1	0	0.0	0	0.0	0	0.0	1	0.5
	Asian - Japanese Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - South East Asian Heritage	0	0.0	0	0.0	0	0.0	1	1.1	0	0.0	1	0.5
	Native Hawaiian or Other Pacific Islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - Arabic / North African Heritage	0	0.0	1	1.1	0	0.0	0	0.0	0	0.0	1	0.5
	White - Caucasian / European Heritage	35	54.7	51	54.3	33	53.2	55	58.5	68	54.0	106	56.4
	Other	6	9.4	7	7.4	4	6.5	7	7.4	10	7.9	14	7.4

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 51 Summary of demographic characteristics by age strata (ATP cohort for immunogenicity)

		Q-QIV				TIV-YB				Total			
		6-17M N = 53		18-35M N = 90		6-17M N = 53		18-35M N = 84		6-17M N = 106		18-35M N = 174	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	10.3	-	26.0	-	10.1	-	26.4	-	10.2	-	26.2	-
	SD	3.5	-	4.9	-	3.3	-	4.9	-	3.4	-	4.9	-
	Median	10.0	-	25.0	-	10.0	-	26.0	-	10.0	-	25.5	-
	Minimum	6	-	18	-	6	-	18	-	6	-	18	-
	Maximum	17	-	35	-	17	-	35	-	17	-	35	-
Gender	Female	23	43.4	44	48.9	29	54.7	42	50.0	52	49.1	86	49.4
	Male	30	56.6	46	51.1	24	45.3	42	50.0	54	50.9	88	50.6
Ethnicity	American Hispanic or Latino	12	22.6	15	16.7	12	22.6	17	20.2	24	22.6	32	18.4
	Not American Hispanic or Latino	41	77.4	75	83.3	41	77.4	67	79.8	82	77.4	142	81.6
Geographic Ancestry	African Heritage / African American	19	35.8	31	34.4	21	39.6	25	29.8	40	37.7	56	32.2
	American Indian or Alaskan Native	0	0.0	1	1.1	0	0.0	0	0.0	0	0.0	1	0.6
	Asian - Central/South Asian Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - East Asian Heritage	0	0.0	1	1.1	0	0.0	0	0.0	0	0.0	1	0.6
	Asian - Japanese Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - South East Asian Heritage	0	0.0	0	0.0	0	0.0	1	1.2	0	0.0	1	0.6
	Native Hawaiian or Other Pacific Islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - Arabic / North African Heritage	0	0.0	1	1.1	0	0.0	0	0.0	0	0.0	1	0.6
	White - Caucasian / European Heritage	31	58.5	49	54.4	28	52.8	51	60.7	59	55.7	100	57.5
	Other	3	5.7	7	7.8	4	7.5	7	8.3	7	6.6	14	8.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 52 Age (in months) at vaccination Dose 1 by gender and by age strata (Total vaccinated cohort)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	6-17M	F	28	28	11.7	3.3	6	17
		M	36	36	9.2	3.2	6	17
		Total	64	64	10.3	3.5	6	17
	18-35M	F	46	46	26.2	5.1	18	35
		M	48	48	25.7	4.7	18	35
		Total	94	94	26.0	4.9	18	35
TIV-YB	6-17M	F	34	34	11.3	3.3	6	17
		M	28	28	8.9	3.1	6	15
		Total	62	62	10.2	3.4	6	17
	18-35M	F	48	48	26.3	4.5	18	35
		M	46	46	25.9	5	18	35
		Total	94	94	26.1	4.8	18	35
ALL	6-17M	F	62	62	11.5	3.3	6	17
		M	64	64	9.1	3.1	6	17
		Total	126	126	10.3	3.4	6	17
	18-35M	F	94	94	26.3	4.8	18	35
		M	94	94	25.8	4.8	18	35
		Total	188	188	26.0	4.8	18	35

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 53 Age (in months) at vaccination Dose 1 by gender and by age strata (ATP cohort for immunogenicity)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	6-17M	F	23	23	12.2	3.1	6	17
		M	30	30	8.8	3.1	6	17
		Total	53	53	10.3	3.5	6	17
	18-35M	F	44	44	26.4	5.1	18	35
		M	46	46	25.6	4.7	18	35
		Total	90	90	26.0	4.9	18	35
TIV-YB	6-17M	F	29	29	11.4	3.2	6	17
		M	24	24	8.5	2.7	6	15
		Total	53	53	10.1	3.3	6	17
	18-35M	F	42	42	26.7	4.6	18	35
		M	42	42	26.1	5.2	18	35
		Total	84	84	26.4	4.9	18	35
ALL	6-17M	F	52	52	11.8	3.1	6	17
		M	54	54	8.6	2.9	6	17
		Total	106	106	10.2	3.4	6	17
	18-35M	F	86	86	26.5	4.8	18	35
		M	88	88	25.8	4.9	18	35
		Total	174	174	26.2	4.9	18	35

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 54 Summary of vital signs characteristics at pre-vaccination by age strata (Total vaccinated cohort)

		Q-QIV		TIV-YB		Total	
		6-17M N = 64	18-35M N = 94	6-17M N = 62	18-35M N = 94	6-17M N = 126	18-35M N = 188
Characteristics	Parameters	Value	Value	Value	Value	Value	Value
Height (cm)	Mean	72.9	88.5	72.6	88.6	72.7	88.5
	SD	4.7	5.6	4.9	5.7	4.8	5.6
	Median	74.0	89.0	74.0	89.0	74.0	89.0
	Minimum	64.0	76.0	63.0	79.0	63.0	76.0
	Maximum	86.0	102.0	81.0	107.0	86.0	107.0
	Unknown	0	1	0	0	0	1
Weight (kg)	Mean	9.7	13.5	9.3	13.4	9.5	13.4
	SD	2.4	3.4	1.4	3.2	2.0	3.3
	Median	9.4	12.9	9.2	12.7	9.3	12.8
	Minimum	7.0	9.7	6.7	9.5	6.7	9.5
	Maximum	24.6	35.0	13.9	34.0	24.6	35.0
	Unknown	0	1	0	0	0	1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 55 History of influenza vaccination in the previous 3 seasons by age strata (Total vaccinated cohort)

		Q-QIV				TIV-YB				Total			
		6-17M N = 64		18-35M N = 94		6-17M N = 62		18-35M N = 94		6-17M N = 126		18-35M N = 188	
Characteristics	Parameters or Categories	n	%	n	%	n	%	n	%	n	%	n	%
At least one season	Yes	3	4.7	71	75.5	5	8.1	67	71.3	8	6.3	138	73.4
	No	61	95.3	23	24.5	57	91.9	27	28.7	118	93.7	50	26.6
Season 2013-2012	Yes	3	4.7	63	67.0	5	8.1	56	59.6	8	6.3	119	63.3
Season 2012-2011	Yes	0	0.0	24	25.5	0	0.0	35	37.2	0	0.0	59	31.4
Season 2011-2010	Yes	0	0.0	1	1.1	0	0.0	3	3.2	0	0.0	4	2.1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N=Total number of subjects
n=number of subjects with influenza vaccination during the specified season
%=n / Number of subjects with available results * 100

Table 56 Study population by age strata (Total vaccinated cohort)

	Q-QIV		TIV-YB		Total	
Number of subjects	**6-17M**	**18-35M**	**6-17M**	**18-35M**	**6-17M**	**18-35M**
Planned, N						
Randomised, N (Total Vaccinated Cohort)	64	94	62	94	126	188
Completed Month 6 visit, n (%)	54 (84.4)	89 (94.7)	54 (87.1)	87 (92.6)	108 (85.7)	176 (93.6)
Demographics	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
N (Total Vaccinated Cohort)	64	94	62	94	126	188
Females:Males	28:36	46:48	34:28	48:46	62:64	94:94
Mean Age, months (SD)	10.3 (3.5)	26.0 (4.9)	10.2 (3.4)	26.1 (4.8)	10.3 (3.4)	26.0 (4.8)
Median Age, months (minimum, maximum)	11 (6, 17)	25 (18, 35)	10 (6, 17)	26 (18, 35)	10 (6, 17)	25 (18, 35)
White - Caucasian / European Heritage, n (%)	35 (54.7)	51 (54.3)	33 (53.2)	55 (58.5)	68 (54.0)	106 (56.4)
African Heritage / African American, n (%)	23 (35.9)	33 (35.1)	25 (40.3)	31 (33.0)	48 (38.1)	64 (34.0)
Others, n (%)	6 (9.4)	7 (7.4)	4 (6.5)	7 (7.4)	10 (7.9)	14 (7.4)

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N=total number of subjects
n/%=number/percentage of subjects
SD=standard deviation

Table 57 Summary of demographic characteristics by priming status (Total vaccinated cohort)

		Q-QIV				TIV-YB				Total			
		UNPRIM N = 101		PRIM N = 57		UNPRIM N = 99		PRIM N = 57		UNPRIM N = 200		PRIM N = 114	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	16.7	-	24.8	-	16.1	-	26.2	-	16.4	-	25.5	-
	SD	9.1	-	5.3	-	8.4	-	5.6	-	8.7	-	5.5	-
	Median	13.0	-	24.0	-	14.0	-	26.0	-	13.0	-	24.5	-
	Minimum	6	-	15	-	6	-	15	-	6	-	15	-
	Maximum	35	-	35	-	34	-	35	-	35	-	35	-
Gender	Female	49	48.5	25	43.9	55	55.6	27	47.4	104	52.0	52	45.6
	Male	52	51.5	32	56.1	44	44.4	30	52.6	96	48.0	62	54.4
Ethnicity	American Hispanic or Latino	24	23.8	5	8.8	28	28.3	4	7.0	52	26.0	9	7.9
	Not American Hispanic or Latino	77	76.2	52	91.2	71	71.7	53	93.0	148	74.0	105	92.1
Geographic Ancestry	African Heritage / African American	37	36.6	19	33.3	40	40.4	16	28.1	77	38.5	35	30.7
	American Indian or Alaskan Native	0	0.0	1	1.8	0	0.0	0	0.0	0	0.0	1	0.9
	Asian - Central/South Asian Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - East Asian Heritage	1	1.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0
	Asian - Japanese Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - South East Asian Heritage	0	0.0	0	0.0	0	0.0	1	1.8	0	0.0	1	0.9
	Native Hawaiian or Other Pacific Islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - Arabic / North African Heritage	0	0.0	1	1.8	0	0.0	0	0.0	0	0.0	1	0.9
	White - Caucasian / European Heritage	56	55.4	30	52.6	53	53.5	35	61.4	109	54.5	65	57.0
	Other	7	6.9	6	10.5	6	6.1	5	8.8	13	6.5	11	9.6

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 58 Summary of demographic characteristics by priming status (ATP cohort for immunogenicity)

		Q-QIV				TIV-YB				Total			
		UNPRIM N = 87		PRIM N = 56		UNPRIM N = 83		PRIM N = 54		UNPRIM N = 170		PRIM N = 110	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	17.1	-	24.9	-	15.9	-	26.5	-	16.5	-	25.7	-
	SD	9.3	-	5.4	-	8.5	-	5.5	-	8.9	-	5.4	-
	Median	14.0	-	24.0	-	12.0	-	27.0	-	13.0	-	25.0	-
	Minimum	6	-	15	-	6	-	15	-	6	-	15	-
	Maximum	35	-	35	-	34	-	35	-	35	-	35	-
Gender	Female	43	49.4	24	42.9	45	54.2	26	48.1	88	51.8	50	45.5
	Male	44	50.6	32	57.1	38	45.8	28	51.9	82	48.2	60	54.5
Ethnicity	American Hispanic or Latino	22	25.3	5	8.9	25	30.1	4	7.4	47	27.6	9	8.2
	Not American Hispanic or Latino	65	74.7	51	91.1	58	69.9	50	92.6	123	72.4	101	91.8
Geographic Ancestry	African Heritage / African American	32	36.8	18	32.1	32	38.6	14	25.9	64	37.6	32	29.1
	American Indian or Alaskan Native	0	0.0	1	1.8	0	0.0	0	0.0	0	0.0	1	0.9
	Asian - Central/South Asian Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - East Asian Heritage	1	1.1	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
	Asian - Japanese Heritage	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Asian - South East Asian Heritage	0	0.0	0	0.0	0	0.0	1	1.9	0	0.0	1	0.9
	Native Hawaiian or Other Pacific Islander	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	White - Arabic / North African Heritage	0	0.0	1	1.8	0	0.0	0	0.0	0	0.0	1	0.9
	White - Caucasian / European Heritage	50	57.5	30	53.6	45	54.2	34	63.0	95	55.9	64	58.2
	Other	4	4.6	6	10.7	6	7.2	5	9.3	10	5.9	11	10.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 59 Age (in months) at vaccination Dose 1 by gender and by priming status (Total vaccinated cohort)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	UNPRIM	F	49	49	18.8	8.8	6	35
		M	52	52	14.7	9	6	34
		Total	101	101	16.7	9.1	6	35
	PRIM	F	25	25	24.4	5.9	15	35
		M	32	32	25.0	5	18	35
		Total	57	57	24.8	5.3	15	35
TIV-YB	UNPRIM	F	55	55	17.5	8.4	6	34
		M	44	44	14.4	8.1	6	33
		Total	99	99	16.1	8.4	6	34
	PRIM	F	27	27	25.3	5.8	15	35
		M	30	30	26.9	5.3	15	35
		Total	57	57	26.2	5.6	15	35
ALL	UNPRIM	F	104	104	18.1	8.6	6	35
		M	96	96	14.6	8.6	6	34
		Total	200	200	16.4	8.7	6	35
	PRIM	F	52	52	24.9	5.8	15	35
		M	62	62	25.9	5.2	15	35
		Total	114	114	25.5	5.5	15	35

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 60 Age (in months) at vaccination Dose 1 by gender and by priming status (ATP cohort for immunogenicity)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	UNPRIM	F	43	43	19.8	8.7	6	35
		M	44	44	14.6	9.2	6	34
		Total	87	87	17.1	9.3	6	35
	PRIM	F	24	24	24.6	6	15	35
		M	32	32	25.0	5	18	35
		Total	56	56	24.9	5.4	15	35
TIV-YB	UNPRIM	F	45	45	17.5	8.6	6	34
		M	38	38	14.0	8.1	6	33
		Total	83	83	15.9	8.5	6	34
	PRIM	F	26	26	25.5	5.9	15	35
		M	28	28	27.4	5	18	35
		Total	54	54	26.5	5.5	15	35
ALL	UNPRIM	F	88	88	18.6	8.7	6	35
		M	82	82	14.3	8.7	6	34
		Total	170	170	16.5	8.9	6	35
	PRIM	F	50	50	25.1	5.9	15	35
		M	60	60	26.2	5.1	18	35
		Total	110	110	25.7	5.4	15	35

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 61 Summary of vital signs characteristics at pre-vaccination by priming status (Total vaccinated cohort)

		Q-QIV		TIV-YB		Total	
		UNPRIM N = 101	PRIM N = 57	UNPRIM N = 99	PRIM N = 57	UNPRIM N = 200	PRIM N = 114
Characteristics	Parameters	Value	Value	Value	Value	Value	Value
Height (cm)	Mean	79.2	87.2	78.8	88.2	79.0	87.7
	SD	9.6	6.1	9.4	6.2	9.4	6.2
	Median	76.0	89.0	76.0	89.0	76.0	89.0
	Minimum	64.0	76.0	63.0	79.0	63.0	76.0
	Maximum	99.0	102.0	103.0	107.0	103.0	107.0
	Unknown	0	1	0	0	0	1
Weight (kg)	Mean	11.4	12.8	11.3	12.6	11.4	12.7
	SD	4.1	2.0	3.9	1.6	4.0	1.8
	Median	10.5	12.6	10.5	12.4	10.5	12.6
	Minimum	7.0	9.9	6.7	9.5	6.7	9.5
	Maximum	35.0	22.4	34.0	16.8	35.0	22.4
	Unknown	0	1	0	0	0	1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 62 History of influenza vaccination in the previous 3 seasons by priming status (Total vaccinated cohort)

		Q-QIV				TIV-YB				Total			
		UNPRIM N = 101		PRIM N = 57		UNPRIM N = 99		PRIM N = 57		UNPRIM N = 200		PRIM N = 114	
Characteristics	Parameters or Categories	n	%	n	%	n	%	n	%	n	%	n	%
At least one season	Yes	17	16.8	57	100	15	15.2	57	100	32	16.0	114	100
	No	84	83.2	0	0.0	84	84.8	0	0.0	168	84.0	0	0.0
Season 2013-2012	Yes	13	12.9	53	93.0	8	8.1	53	93.0	21	10.5	106	93.0
Season 2012-2011	Yes	4	4.0	20	35.1	7	7.1	28	49.1	11	5.5	48	42.1
Season 2011-2010	Yes	0	0.0	1	1.8	0	0.0	3	5.3	0	0.0	4	3.5

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N=Total number of subjects
n=number of subjects with influenza vaccination during the specified season
%=n / Number of subjects with available results * 100

Table 63 Study population by priming status (Total vaccinated cohort)

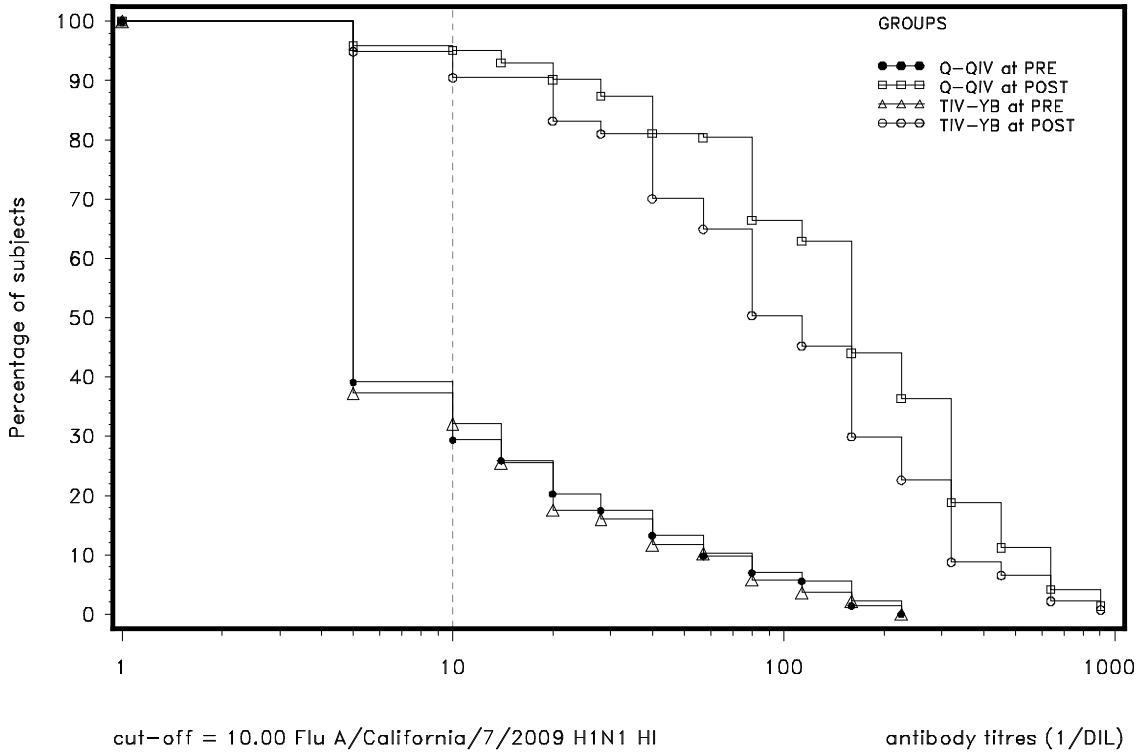
	Q-QIV		TIV-YB		Total	
Number of subjects	**UNPRIM**	**PRIM**	**UNPRIM**	**PRIM**	**UNPRIM**	**PRIM**
Planned, N						
Randomised, N (Total Vaccinated Cohort)	101	57	99	57	200	114
Completed Month 6 visit, n (%)	89 (88.1)	54 (94.7)	88 (88.9)	53 (93.0)	177 (88.5)	107 (93.9)
Demographics	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
N (Total Vaccinated Cohort)	101	57	99	57	200	114
Females:Males	49:52	25:32	55:44	27:30	104:96	52:62
Mean Age, months (SD)	16.7 (9.1)	24.8 (5.3)	16.1 (8.4)	26.2 (5.6)	16.4 (8.7)	25.5 (5.5)
Median Age, months (minimum, maximum)	13 (6, 35)	24 (15, 35)	14 (6, 34)	26 (15, 35)	13 (6, 35)	25 (15, 35)
White - Caucasian / European Heritage, n (%)	56 (55.4)	30 (52.6)	53 (53.5)	35 (61.4)	109 (54.5)	65 (57.0)
African Heritage / African American, n (%)	37 (36.6)	19 (33.3)	40 (40.4)	16 (28.1)	77 (38.5)	35 (30.7)
Others, n (%)	7 (6.9)	6 (10.5)	6 (6.1)	5 (8.8)	13 (6.5)	11 (9.6)

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N=total number of subjects
n/%=number/percentage of subjects
SD=standard deviation

10.2. Immunogenicity

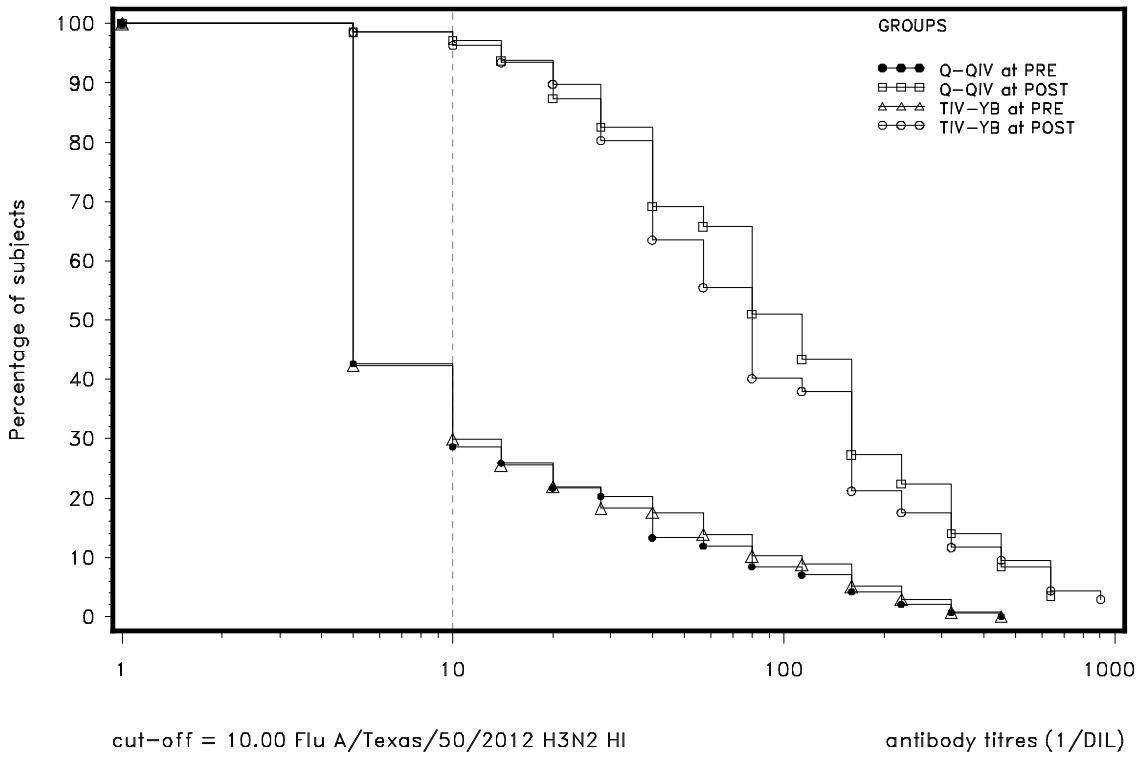
10.2.1. ATP cohort for immunogenicity

Figure 1 Reverse cumulative distribution curves of Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)



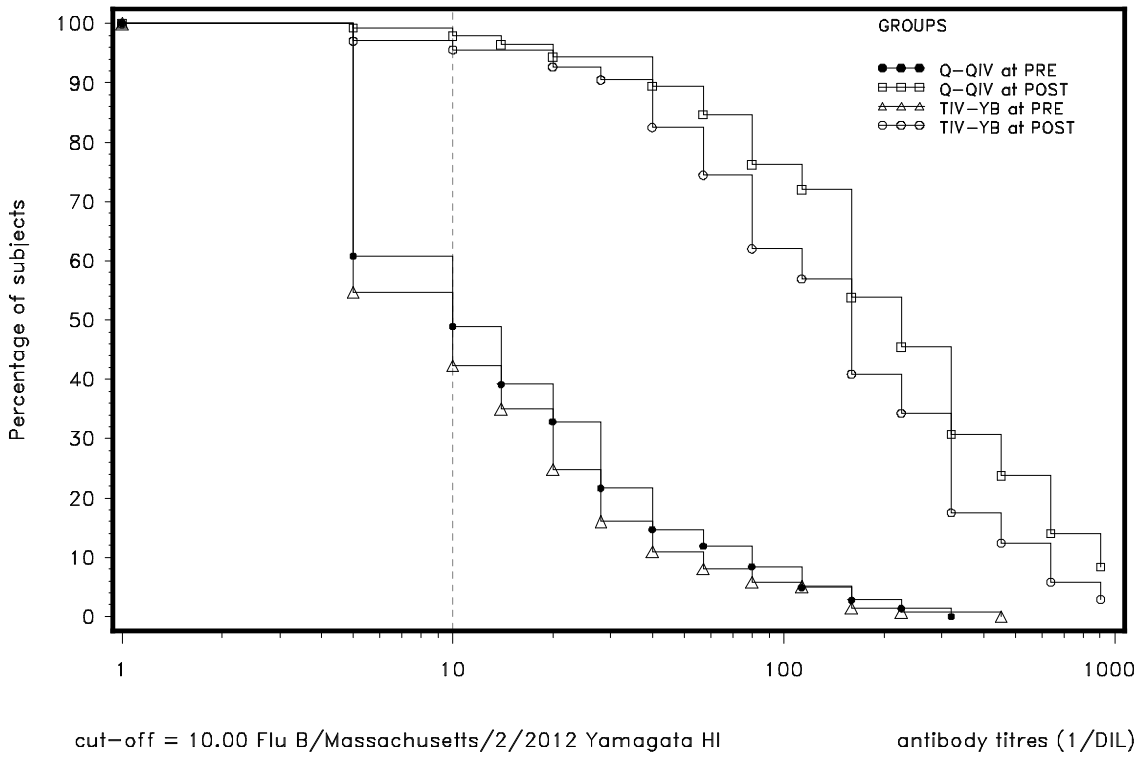
Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

Figure 2 Reverse cumulative distribution curves of Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)



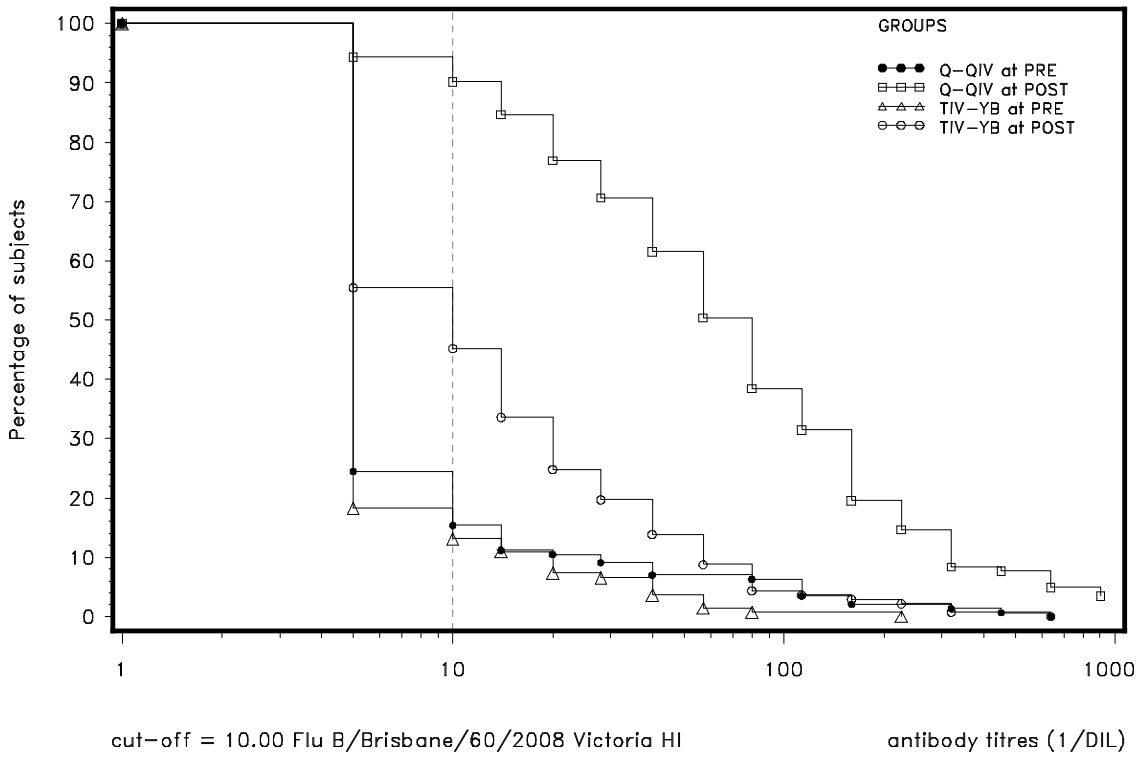
Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

Figure 3 Reverse cumulative distribution curves of Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

Figure 4 Reverse cumulative distribution curves of Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

Table 64 Seropositivity rates, seroprotection rates (SPR) and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by age strata (ATP cohort for immunogenicity)

					≥ 10 1/DIL				≥ 40 1/DIL				GMT				
							95% CI				95% CI			95% CI			
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu A/California/7/2009 H1N1 HI	Q-QIV	6-17M	PRE	53	5	9.4	3.1	20.7	3	5.7	1.2	15.7	6.1	5.0	7.4	<10.0	160.0
			POST	53	47	88.7	77.0	95.7	36	67.9	53.7	80.1	68.3	46.0	101.4	<10.0	1280.0
		18-35M	PRE	90	51	56.7	45.8	67.1	22	24.4	16.0	34.6	14.0	10.9	17.9	<10.0	226.0
			POST	90	90	100	96.0	100	89	98.9	94.0	100	216.9	180.9	260.0	10.0	1280.0
	TIV-YB	6-17M	PRE	53	8	15.1	6.7	27.6	4	7.5	2.1	18.2	6.5	5.3	7.9	<10.0	113.0
			POST	53	47	88.7	77.0	95.7	37	69.8	55.7	81.7	54.0	37.9	77.1	<10.0	640.0
		18-35M	PRE	84	43	51.2	40.0	62.3	18	21.4	13.2	31.7	13.1	10.1	16.8	<10.0	226.0
			POST	84	83	98.8	93.5	100	74	88.1	79.2	94.1	126.0	98.0	161.8	<10.0	1280.0
Flu A/Texas/50/2012 H3N2 HI	Q-QIV	6-17M	PRE	53	11	20.8	10.8	34.1	4	7.5	2.1	18.2	7.2	5.6	9.1	<10.0	226.0
			POST	53	51	96.2	87.0	99.5	32	60.4	46.0	73.5	52.2	36.7	74.3	<10.0	1280.0
		18-35M	PRE	90	50	55.6	44.7	66.0	25	27.8	18.9	38.2	14.3	11.0	18.7	<10.0	453.0
			POST	90	90	100	96.0	100	86	95.6	89.0	98.8	148.1	121.4	180.7	20.0	1280.0
	TIV-YB	6-17M	PRE	53	9	17.0	8.1	29.8	3	5.7	1.2	15.7	6.8	5.3	8.8	<10.0	320.0
			POST	53	52	98.1	89.9	100	37	69.8	55.7	81.7	58.7	43.3	79.6	<10.0	905.0
		18-35M	PRE	84	49	58.3	47.1	69.0	22	26.2	17.2	36.9	15.9	11.9	21.2	<10.0	453.0
			POST	84	83	98.8	93.5	100	73	86.9	77.8	93.3	109.9	85.0	142.0	<10.0	1810.0
Flu B/Massachusetts/2/2012 Yamagata HI	Q-QIV	6-17M	PRE	53	26	49.1	35.1	63.2	6	11.3	4.3	23.0	10.4	7.8	13.7	<10.0	320.0
			POST	53	52	98.1	89.9	100	45	84.9	72.4	93.3	101.9	71.8	144.7	<10.0	1280.0
		18-35M	PRE	90	61	67.8	57.1	77.2	25	27.8	18.9	38.2	17.7	14.0	22.5	<10.0	320.0
			POST	90	90	100	96.0	100	90	100	96.0	100	326.2	272.4	390.7	57.0	1810.0
	TIV-YB	6-17M	PRE	53	20	37.7	24.8	52.1	5	9.4	3.1	20.7	8.4	6.8	10.4	<10.0	113.0
			POST	53	49	92.5	81.8	97.9	42	79.2	65.9	89.2	70.7	51.4	97.3	<10.0	320.0
		18-35M	PRE	84	55	65.5	54.3	75.5	17	20.2	12.3	30.4	15.7	12.3	20.1	<10.0	453.0
			POST	84	84	100	95.7	100	82	97.6	91.7	99.7	215.4	171.3	270.8	20.0	2560.0

					≥ 10 1/DIL				≥ 40 1/DIL				GMT				
							95% CI				95% CI			95% CI			
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu B/Brisbane/60/2008 Victoria HI	Q-QIV	6-17M	PRE	53	7	13.2	5.5	25.3	0	0.0	0.0	6.7	5.6	5.2	6.1	<10.0	14.0
			POST	53	48	90.6	79.3	96.9	32	60.4	46.0	73.5	45.8	32.9	63.9	<10.0	453.0
		18-35M	PRE	90	28	31.1	21.8	41.7	13	14.4	7.9	23.4	9.3	7.3	12.0	<10.0	640.0
			POST	90	87	96.7	90.6	99.3	69	76.7	66.6	84.9	87.7	65.1	118.2	<10.0	3620.0
	TIV-YB	6-17M	PRE	53	4	7.5	2.1	18.2	1	1.9	0.0	10.1	5.5	5.0	6.1	<10.0	40.0
			POST	53	20	37.7	24.8	52.1	2	3.8	0.5	13.0	7.6	6.4	9.0	<10.0	57.0
		18-35M	PRE	84	21	25.0	16.2	35.6	8	9.5	4.2	17.9	7.5	6.3	8.9	<10.0	226.0
			POST	84	56	66.7	55.5	76.6	25	29.8	20.3	40.7	17.8	13.7	23.1	<10.0	640.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
seropositivity=HI antibody titre ≥ 10 1/DIL
seroprotection=HI antibody titre ≥ 40 1/DIL
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Table 65 Seroconversion rate (SCR) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for FLU Q-QIV and FLU TIV-YB by age strata (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Antibody	**Group**	**Sub-group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	6-17M	53	34	64.2	49.8	76.9
		18-35M	90	81	90.0	81.9	95.3
	TIV-YB	6-17M	53	35	66.0	51.7	78.5
		18-35M	84	63	75.0	64.4	83.8
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	6-17M	53	30	56.6	42.3	70.2
		18-35M	90	73	81.1	71.5	88.6
	TIV-YB	6-17M	53	36	67.9	53.7	80.1
		18-35M	84	58	69.0	58.0	78.7
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	6-17M	53	38	71.7	57.7	83.2
		18-35M	90	85	94.4	87.5	98.2
	TIV-YB	6-17M	53	39	73.6	59.7	84.7
		18-35M	84	76	90.5	82.1	95.8
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	6-17M	53	32	60.4	46.0	73.5
		18-35M	90	63	70.0	59.4	79.2
	TIV-YB	6-17M	53	1	1.9	0.0	10.1
		18-35M	84	16	19.0	11.3	29.1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 66 Mean geometric increase (MGI) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose by age strata (ATP cohort for immunogenicity)

								MGI ratio			
										95% CI	
Antibody	Group	Sub-group	N	Time point description	MGI	Time point description	MGI	Ratio order	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	6-17M	53	POST	68.3	PRE	6.1	POST / PRE	11.15	7.26	17.12
		18-35M	90	POST	216.9	PRE	14.0	POST / PRE	15.53	12.35	19.52
	TIV-YB	6-17M	53	POST	54.0	PRE	6.5	POST / PRE	8.32	5.68	12.20
		18-35M	84	POST	126.0	PRE	13.1	POST / PRE	9.64	7.38	12.60
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	6-17M	53	POST	52.2	PRE	7.2	POST / PRE	7.29	5.42	9.80
		18-35M	90	POST	148.1	PRE	14.3	POST / PRE	10.36	8.46	12.67
	TIV-YB	6-17M	53	POST	58.7	PRE	6.8	POST / PRE	8.59	6.51	11.33
		18-35M	84	POST	109.9	PRE	15.9	POST / PRE	6.93	5.60	8.58
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	6-17M	53	POST	101.9	PRE	10.4	POST / PRE	9.81	6.22	15.48
		18-35M	90	POST	326.2	PRE	17.7	POST / PRE	18.42	14.85	22.86
	TIV-YB	6-17M	53	POST	70.7	PRE	8.4	POST / PRE	8.44	5.51	12.94
		18-35M	84	POST	215.4	PRE	15.7	POST / PRE	13.70	10.75	17.46
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	6-17M	53	POST	45.8	PRE	5.6	POST / PRE	8.21	5.81	11.60
		18-35M	90	POST	87.7	PRE	9.3	POST / PRE	9.41	7.38	11.99
	TIV-YB	6-17M	53	POST	7.6	PRE	5.5	POST / PRE	1.38	1.18	1.62
		18-35M	84	POST	17.8	PRE	7.5	POST / PRE	2.38	2.00	2.83

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
MGI = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Table 67 Seropositivity rates, seroprotection rates (SPR) and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by priming status (ATP cohort for immunogenicity)

					≥ 10 1/DIL				≥ 40 1/DIL				GMT				
							95% CI				95% CI			95% CI			
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu A/California/7/2009 H1N1 HI	Q-QIV	UNPRIM	PRE	87	20	23.0	14.6	33.2	10	11.5	5.7	20.1	7.8	6.3	9.6	<10.0	226.0
			POST	87	81	93.1	85.6	97.4	70	80.5	70.6	88.2	103.5	77.8	137.9	<10.0	1280.0
		PRIM	PRE	56	36	64.3	50.4	76.6	15	26.8	15.8	40.3	15.9	11.7	21.7	<10.0	160.0
			POST	56	56	100	93.6	100	55	98.2	90.4	100	229.1	181.4	289.4	10.0	905.0
	TIV-YB	UNPRIM	PRE	83	14	16.9	9.5	26.7	4	4.8	1.3	11.9	6.7	5.6	7.9	<10.0	226.0
			POST	83	76	91.6	83.4	96.5	62	74.7	64.0	83.6	74.8	55.4	101.1	<10.0	905.0
		PRIM	PRE	54	37	68.5	54.4	80.5	18	33.3	21.1	47.5	18.5	13.5	25.4	<10.0	226.0
			POST	54	54	100	93.4	100	49	90.7	79.7	96.9	122.2	92.1	162.1	10.0	1280.0
Flu A/Texas/50/2012 H3N2 HI	Q-QIV	UNPRIM	PRE	87	19	21.8	13.7	32.0	10	11.5	5.7	20.1	7.8	6.3	9.8	<10.0	320.0
			POST	87	85	97.7	91.9	99.7	65	74.7	64.3	83.4	75.3	57.2	99.2	<10.0	1280.0
		PRIM	PRE	56	42	75.0	61.6	85.6	19	33.9	21.8	47.8	19.0	13.8	26.3	<10.0	453.0
			POST	56	56	100	93.6	100	53	94.6	85.1	98.9	158.0	125.8	198.3	28.0	1280.0
	TIV-YB	UNPRIM	PRE	83	22	26.5	17.4	37.3	13	15.7	8.6	25.3	9.5	7.1	12.6	<10.0	453.0
			POST	83	82	98.8	93.5	100	65	78.3	67.9	86.6	89.1	67.1	118.2	<10.0	1810.0
		PRIM	PRE	54	36	66.7	52.5	78.9	12	22.2	12.0	35.6	15.4	11.4	20.7	<10.0	226.0
			POST	54	53	98.1	90.1	100	45	83.3	70.7	92.1	82.1	62.3	108.1	<10.0	640.0
Flu B/Massachusetts/2/2012 Yamagata HI	Q-QIV	UNPRIM	PRE	87	39	44.8	34.1	55.9	16	18.4	10.9	28.1	11.4	8.9	14.7	<10.0	320.0
			POST	87	86	98.9	93.8	100	79	90.8	82.7	95.9	158.8	121.1	208.1	<10.0	1280.0
		PRIM	PRE	56	48	85.7	73.8	93.6	15	26.8	15.8	40.3	21.2	16.6	27.0	<10.0	320.0
			POST	56	56	100	93.6	100	56	100	93.6	100	332.1	266.0	414.8	57.0	1810.0
	TIV-YB	UNPRIM	PRE	83	29	34.9	24.8	46.2	8	9.6	4.3	18.1	8.7	7.0	10.8	<10.0	453.0
			POST	83	79	95.2	88.1	98.7	72	86.7	77.5	93.2	111.8	84.0	148.7	<10.0	2560.0
		PRIM	PRE	54	46	85.2	72.9	93.4	14	25.9	15.0	39.7	21.0	16.4	26.9	<10.0	160.0
			POST	54	54	100	93.4	100	52	96.3	87.3	99.5	197.8	151.1	258.8	20.0	2560.0

					≥ 10 1/DIL				≥ 40 1/DIL				GMT				
							95% CI				95% CI			95% CI			
Antibody	**Group**	**Sub-group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu B/Brisbane/60/2008 Victoria HI	Q-QIV	UNPRIM	PRE	87	14	16.1	9.1	25.5	4	4.6	1.3	11.4	6.6	5.5	7.8	<10.0	453.0
			POST	87	82	94.3	87.1	98.1	65	74.7	64.3	83.4	71.5	55.0	93.0	<10.0	3620.0
		PRIM	PRE	56	21	37.5	24.9	51.5	9	16.1	7.6	28.3	9.9	7.2	13.6	<10.0	640.0
			POST	56	53	94.6	85.1	98.9	36	64.3	50.4	76.6	65.2	42.5	99.9	<10.0	3620.0
	TIV-YB	UNPRIM	PRE	83	7	8.4	3.5	16.6	2	2.4	0.3	8.4	5.7	5.1	6.3	<10.0	226.0
			POST	83	37	44.6	33.7	55.9	7	8.4	3.5	16.6	9.1	7.6	11.0	<10.0	320.0
		PRIM	PRE	54	18	33.3	21.1	47.5	7	13.0	5.4	24.9	8.5	6.7	10.7	<10.0	80.0
			POST	54	39	72.2	58.4	83.5	20	37.0	24.3	51.3	21.5	15.3	30.0	<10.0	640.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
seropositivity=HI antibody titre ≥ 10 1/DIL
seroprotection=HI antibody titre ≥ 40 1/DIL
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Table 68 Seroconversion rate (SCR) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for FLU Q-QIV and FLU TIV-YB by priming status (ATP cohort for immunogenicity)

				SCR			
						95% CI	
Antibody	**Group**	**Sub-group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	UNPRIM	87	67	77.0	66.8	85.4
		PRIM	56	48	85.7	73.8	93.6
	TIV-YB	UNPRIM	83	60	72.3	61.4	81.6
		PRIM	54	38	70.4	56.4	82.0
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	UNPRIM	87	63	72.4	61.8	81.5
		PRIM	56	40	71.4	57.8	82.7
	TIV-YB	UNPRIM	83	60	72.3	61.4	81.6
		PRIM	54	34	63.0	48.7	75.7
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	UNPRIM	87	71	81.6	71.9	89.1
		PRIM	56	52	92.9	82.7	98.0
	TIV-YB	UNPRIM	83	68	81.9	72.0	89.5
		PRIM	54	47	87.0	75.1	94.6
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	UNPRIM	87	63	72.4	61.8	81.5
		PRIM	56	32	57.1	43.2	70.3
	TIV-YB	UNPRIM	83	5	6.0	2.0	13.5
		PRIM	54	12	22.2	12.0	35.6

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 69 Mean geometric increase (MGI) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose by priming status (ATP cohort for immunogenicity)

								MGI ratio			
										95% CI	
Antibody	Group	Sub-group	N	Time point description	MGI	Time point description	MGI	Ratio order	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	UNPRIM	87	POST	103.5	PRE	7.8	POST / PRE	13.31	10.04	17.66
		PRIM	56	POST	229.1	PRE	15.9	POST / PRE	14.41	10.35	20.08
	TIV-YB	UNPRIM	83	POST	74.8	PRE	6.7	POST / PRE	11.23	8.28	15.22
		PRIM	54	POST	122.2	PRE	18.5	POST / PRE	6.61	4.97	8.78
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	UNPRIM	87	POST	75.3	PRE	7.8	POST / PRE	9.64	7.75	12.00
		PRIM	56	POST	158.0	PRE	19.0	POST / PRE	8.30	6.35	10.87
	TIV-YB	UNPRIM	83	POST	89.1	PRE	9.5	POST / PRE	9.41	7.59	11.66
		PRIM	54	POST	82.1	PRE	15.4	POST / PRE	5.35	4.17	6.86
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	UNPRIM	87	POST	158.8	PRE	11.4	POST / PRE	13.93	10.15	19.13
		PRIM	56	POST	332.1	PRE	21.2	POST / PRE	15.67	11.87	20.68
	TIV-YB	UNPRIM	83	POST	111.8	PRE	8.7	POST / PRE	12.84	9.25	17.82
		PRIM	54	POST	197.8	PRE	21.0	POST / PRE	9.41	7.26	12.21
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	UNPRIM	87	POST	71.5	PRE	6.6	POST / PRE	10.92	8.45	14.11
		PRIM	56	POST	65.2	PRE	9.9	POST / PRE	6.56	4.86	8.85
	TIV-YB	UNPRIM	83	POST	9.1	PRE	5.7	POST / PRE	1.61	1.39	1.88
		PRIM	54	POST	21.5	PRE	8.5	POST / PRE	2.54	2.04	3.14

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
UNPRIM = Unprimed subjects
PRIM = Primed subjects
MGI = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

10.2.2. Total Vaccinated cohort

Table 70 Seropositivity rates, seroprotection rates (SPR) and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose (Total vaccinated cohort)

				≥ 10 1/DIL				≥ 40 1/DIL				GMT				
						95% CI				95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu A/California/7/2009 H1N1 HI	Q-QIV	PRE	158	60	38.0	30.4	46.0	26	16.5	11.0	23.2	9.9	8.4	11.7	<10.0	226.0
		POST	145	139	95.9	91.2	98.5	127	87.6	81.1	92.5	140.9	115.1	172.5	<10.0	1280.0
	TIV-YB	PRE	156	54	34.6	27.2	42.6	23	14.7	9.6	21.3	9.4	8.0	11.1	<10.0	226.0
		POST	143	136	95.1	90.2	98.0	115	80.4	73.0	86.6	90.5	73.1	112.0	<10.0	1280.0
Flu A/Texas/50/2012 H3N2 HI	Q-QIV	PRE	158	63	39.9	32.2	48.0	31	19.6	13.7	26.7	10.6	8.8	12.7	<10.0	453.0
		POST	145	143	98.6	95.1	99.8	120	82.8	75.6	88.5	101.3	83.2	123.3	<10.0	1280.0
	TIV-YB	PRE	156	64	41.0	33.2	49.2	29	18.6	12.8	25.6	11.3	9.3	13.8	<10.0	453.0
		POST	143	141	98.6	95.0	99.8	115	80.4	73.0	86.6	87.0	71.3	106.2	<10.0	1810.0
Flu B/Massachusetts/2/2012 Yamagata HI	Q-QIV	PRE	158	93	58.9	50.8	66.6	31	19.6	13.7	26.7	13.7	11.5	16.2	<10.0	320.0
		POST	145	144	99.3	96.2	100	137	94.5	89.4	97.6	211.7	174.8	256.2	<10.0	1810.0
	TIV-YB	PRE	156	86	55.1	47.0	63.1	26	16.7	11.2	23.5	12.8	10.7	15.3	<10.0	453.0
		POST	143	139	97.2	93.0	99.2	129	90.2	84.1	94.5	141.8	115.6	173.9	<10.0	2560.0
Flu B/Brisbane/60/2008 Victoria HI	Q-QIV	PRE	158	35	22.2	15.9	29.4	13	8.2	4.5	13.7	7.4	6.4	8.6	<10.0	640.0
		POST	145	137	94.5	89.4	97.6	103	71.0	62.9	78.3	69.3	55.3	86.8	<10.0	3620.0
	TIV-YB	PRE	156	29	18.6	12.8	25.6	10	6.4	3.1	11.5	6.6	5.9	7.4	<10.0	226.0
		POST	143	79	55.2	46.7	63.6	29	20.3	14.0	27.8	13.0	10.8	15.7	<10.0	640.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
seropositivity=HI antibody titre ≥ 10 1/DIL
seroprotection=HI antibody titre ≥ 40 1/DIL
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Table 71 Seroconversion rate (SCR) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for FLU Q-QIV and FLU TIV-YB (Total vaccinated cohort)

			SCR			
					95% CI	
Antibody	**Group**	**N**	**n**	**%**	**LL**	**UL**
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	145	117	80.7	73.3	86.8
	TIV-YB	143	102	71.3	63.2	78.6
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	145	105	72.4	64.4	79.5
	TIV-YB	143	98	68.5	60.2	76.0
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	145	125	86.2	79.5	91.4
	TIV-YB	143	120	83.9	76.9	89.5
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	145	97	66.9	58.6	74.5
	TIV-YB	143	19	13.3	8.2	20.0

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 72 Mean geometric increase (MGI) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose (Total vaccinated cohort)

							MGI ratio			
									95% CI	
Antibody	Group	N	Time point description	MGI	Time point description	MGI	Ratio order	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	145	POST	140.9	PRE	10.2	POST / PRE	13.76	11.15	16.98
	TIV-YB	143	POST	90.5	PRE	9.7	POST / PRE	9.35	7.53	11.61
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	145	POST	101.3	PRE	11.1	POST / PRE	9.10	7.71	10.74
	TIV-YB	143	POST	87.0	PRE	11.5	POST / PRE	7.55	6.40	8.90
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	145	POST	211.7	PRE	14.5	POST / PRE	14.57	11.74	18.09
	TIV-YB	143	POST	141.8	PRE	12.4	POST / PRE	11.47	9.22	14.27
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	145	POST	69.3	PRE	7.7	POST / PRE	9.04	7.43	10.99
	TIV-YB	143	POST	13.0	PRE	6.6	POST / PRE	1.96	1.71	2.25

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
MGI = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titre to the Day 0 reciprocal HI titre
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Table 73 Adjusted GMT ratios of B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: Q-QIV/TIV-YB (Total vaccinated cohort)

				Adjusted GMT ratio (Q-QIV / TIV-YB)		
Q-QIV		TIV-YB			95% CI	
N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
145	65.1	143	13.9	4.70	3.70	5.95

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 74 SCR Difference between groups for B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: Q-QIV minus TIV-YB (Total vaccinated cohort)

							Difference in SCR (Q-QIV minus TIV-YB)		
	Q-QIV			TIV-YB				95% CI	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	145	97	66.9	143	19	13.3	53.61	43.53	62.43

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as:
For initially seronegative subjects: post-vaccination antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 75 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata) at 28 days after the last vaccine dose: TIV-YB/Q-QIV (Total vaccinated cohort)

					Adjusted GMT ratio (TIV-YB / Q-QIV)		
	TIV-YB		Q-QIV			95% CI	
Antibody	**N**	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
Flu A/California/7/2009 H1N1 HI (1/DIL)	143	91.7	145	139.1	0.66	0.50	0.86
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	143	86.0	145	102.4	0.84	0.68	1.04
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	143	146.2	145	205.4	0.71	0.55	0.93

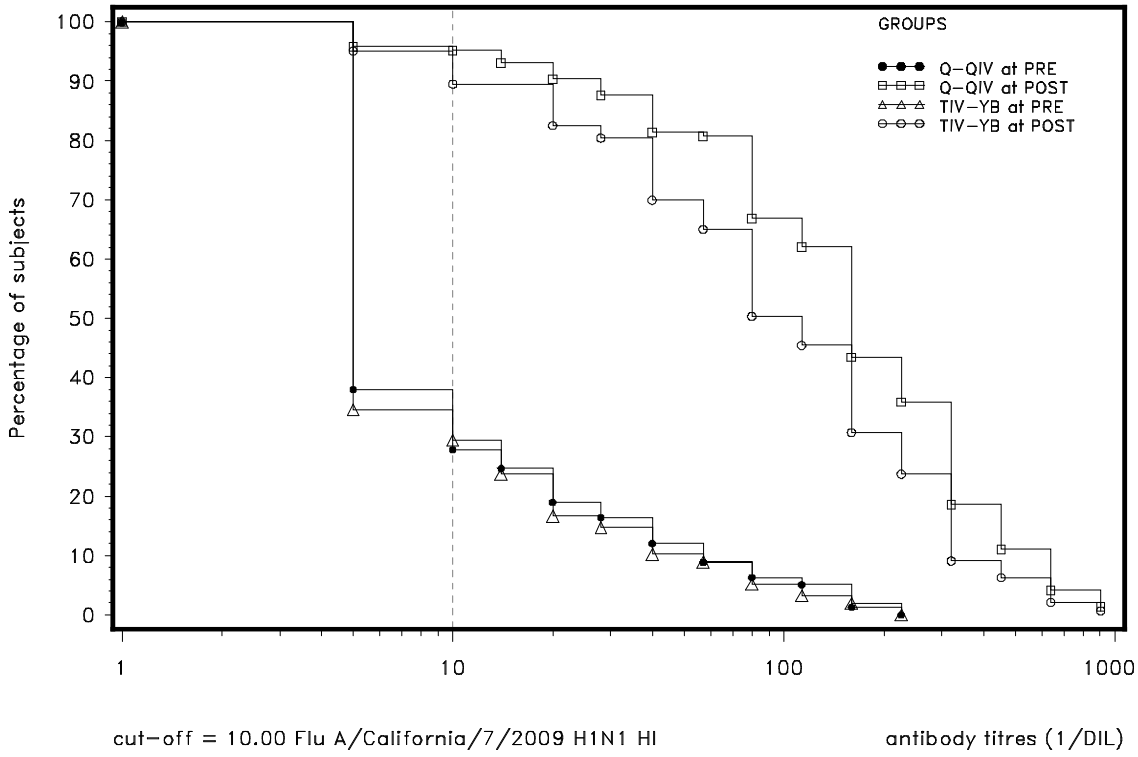
Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 76 SCR difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata) at 28 days after the last vaccine dose: TIV-YB minus Q-QIV (Total vaccinated cohort)

							Difference in SCR (TIV-YB minus Q-QIV)		
	TIV-YB			Q-QIV				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	143	102	71.3	145	117	80.7	-9.36	-19.18	0.52
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	143	98	68.5	145	105	72.4	-3.88	-14.39	6.67
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	143	120	83.9	145	125	86.2	-2.29	-10.72	6.07

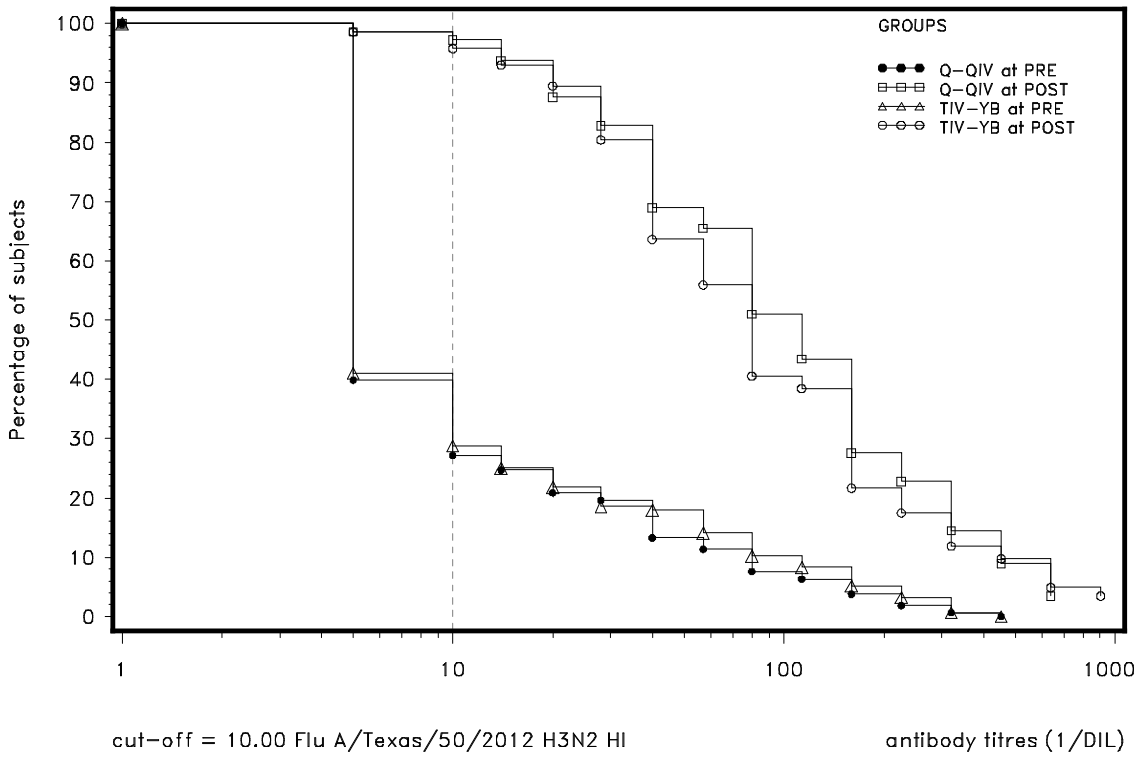
Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SCR defined as:
For initially seronegative subjects: post-vaccination antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects: antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Figure 5 Reverse cumulative distribution curves of Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose (Total vaccinated cohort)



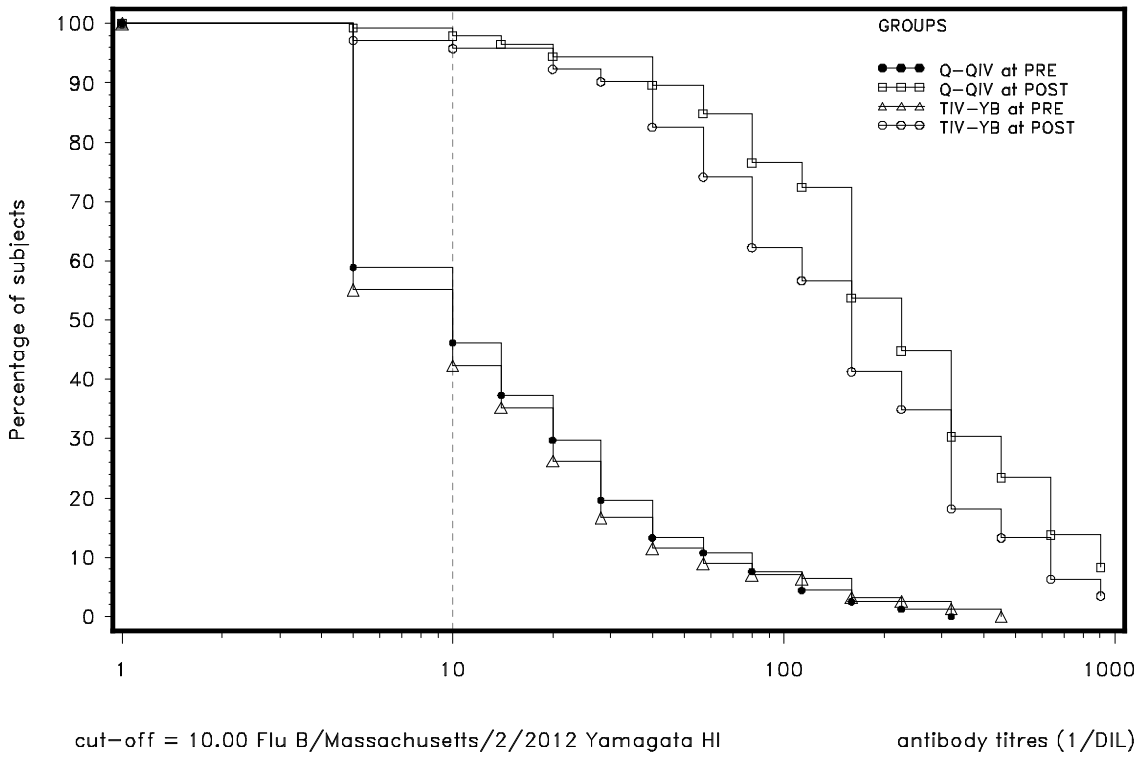
Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

Figure 6 Reverse cumulative distribution curves of Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose (Total vaccinated cohort)



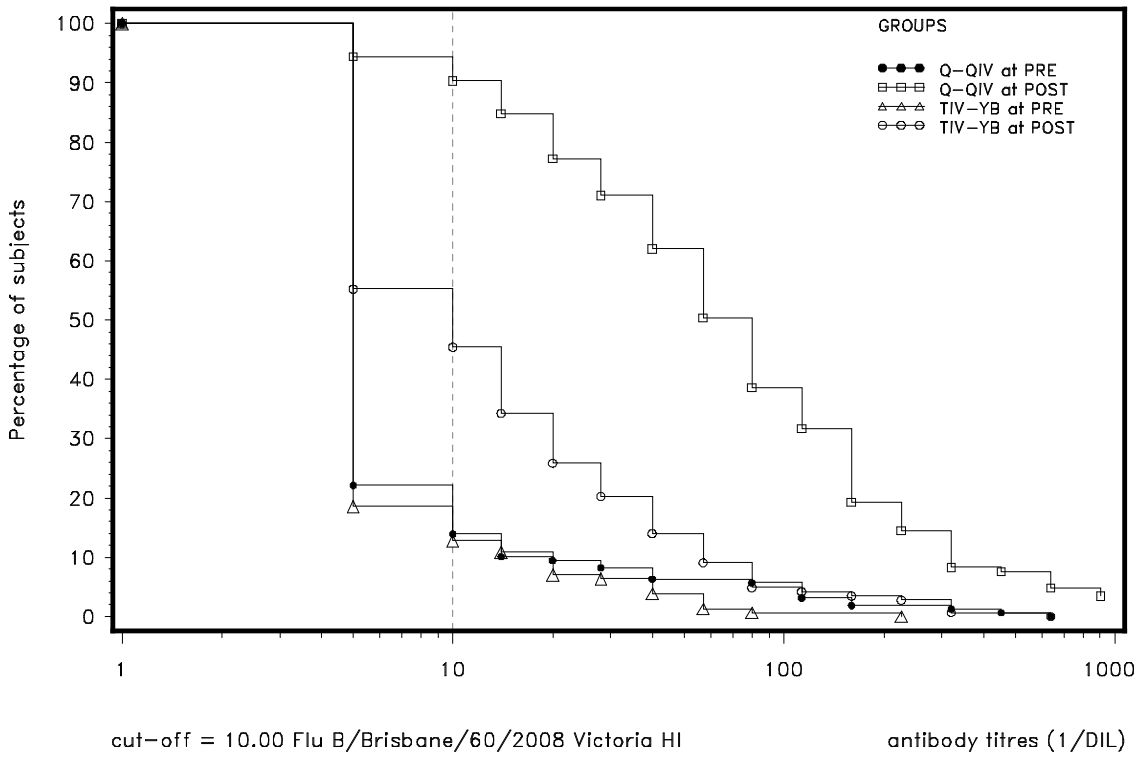
Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

Figure 7 Reverse cumulative distribution curves of Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose (Total vaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

Figure 8 Reverse cumulative distribution curves of Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose (Total vaccinated cohort)



Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
PRE=Pre-vaccination at Day 0
POST=28 days Post last vaccination (Day 28 or Day 56)

10.3. Safety

10.3.1. Total Vaccinated cohort

Table 77 Compliance in returning symptom sheets (Total vaccinated cohort)

Dose	Group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
1	Q-QIV	158	21	150	94.9	150	94.9
	TIV-YB	156	15	147	94.2	147	94.2
2	Q-QIV	94	6	89	94.7	89	94.7
	TIV-YB	92	5	89	96.7	89	96.7
Total	Q-QIV	252	27	239	94.8	239	94.8
	TIV-YB	248	20	236	95.2	236	95.2

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Table 78 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		77	48.7	40.7	56.8	75	48.1	40.0	56.2
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Cardiac disorders (10007541)	Cyanosis (10011703)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Eye disorders (10015919)	Conjunctival haemorrhage (10010719)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Eye pruritus (10052140)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Lacrimation increased (10023644)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.6	0.0	3.5	2	1.3	0.2	4.6
	Diarrhoea (10012735)	15	9.5	5.4	15.2	4	2.6	0.7	6.4
	Nausea (10028813)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Teething (10043183)	1	0.6	0.0	3.5	4	2.6	0.7	6.4
	Vomiting (10047700)	9	5.7	2.6	10.5	7	4.5	1.8	9.0
General disorders and administration site conditions (10018065)	Injection site bruising (10022052)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Pyrexia (10037660)	7	4.4	1.8	8.9	6	3.8	1.4	8.2
Immune system disorders (10021428)	Allergy to arthropod bite (10058285)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Milk allergy (10027633)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Infections and infestations (10021881)	Acrodermatitis (10063409)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Adenovirus infection (10060931)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Bronchiolitis (10006448)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Bronchitis (10006451)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Carbuncle (10007247)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Conjunctivitis (10010741)	1	0.6	0.0	3.5	4	2.6	0.7	6.4
	Croup infectious (10011416)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Ear infection (10014011)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Folliculitis (10016936)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Furuncle (10017553)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Gastroenteritis (10017888)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Nasopharyngitis (10028810)	8	5.1	2.2	9.7	9	5.8	2.7	10.7
	Onychomycosis (10030338)	1	0.6	0.0	3.5	0	0.0	0.0	2.3

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Oral candidiasis (10030963)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Otitis media (10033078)	11	7.0	3.5	12.1	12	7.7	4.0	13.1
	Otitis media acute (10033079)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Paronychia (10034016)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Pharyngitis (10034835)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Pharyngotonsillitis (10049140)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Respiratory syncytial virus infection (10061603)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Rhinitis (10039083)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Sinusitis (10040753)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Staphylococcal abscess (10041917)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Tinea infection (10060889)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Tonsillitis (10044008)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Upper respiratory tract infection (10046306)	11	7.0	3.5	12.1	11	7.1	3.6	12.3
	Viral infection (10047461)	5	3.2	1.0	7.2	6	3.8	1.4	8.2
	Viral rash (10047476)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Viral upper respiratory tract infection (10047482)	3	1.9	0.4	5.4	6	3.8	1.4	8.2
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Contusion (10050584)	1	0.6	0.0	3.5	2	1.3	0.2	4.6
	Foreign body (10070245)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Head injury (10019196)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
	Laceration (10023572)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Investigations (10022891)	Cardiac murmur (10007586)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	2	1.3	0.2	4.5	0	0.0	0.0	2.3
	Lactose intolerance (10023681)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Musculoskeletal and connective tissue disorders (10028395)	Muscular weakness (10028372)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Nervous system disorders (10029205)	Dizziness (10013573)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Self-induced vomiting (10048636)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Sleep terror (10041010)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Tic (10043833)	1	0.6	0.0	3.5	0	0.0	0.0	2.3

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Bronchial hyperreactivity (10066091)	1	0.6`	0.0	3.5	1	0.6	0.0	3.5
	Cough (10011224)	14	8.9	4.9	14.4	13	8.3	4.5	13.8
	Nasal congestion (10028735)	7	4.4	1.8	8.9	4	2.6	0.7	6.4
	Oropharyngeal pain (10068319)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Rhinorrhoea (10039101)	13	8.2	4.5	13.7	12	7.7	4.0	13.1
	Sneezing (10041232)	3	1.9	0.4	5.4	5	3.2	1.0	7.3
	Wheezing (10047924)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Dermatitis (10012431)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Dermatitis diaper (10012444)	2	1.3	0.2	4.5	2	1.3	0.2	4.6
	Dry skin (10013786)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Eczema (10014184)	2	1.3	0.2	4.5	0	0.0	0.0	2.3
	Hyperhidrosis (10020642)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Rash (10037844)	3	1.9	0.4	5.4	2	1.3	0.2	4.6
	Rash macular (10037867)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Skin lesion (10040882)	1	0.6	0.0	3.5	0	0.0	0.0	2.3

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 79 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 252				TIV-YB N = 248			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		93	36.9	30.9	43.2	93	37.5	31.5	43.8
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Cardiac disorders (10007541)	Cyanosis (10011703)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Eye disorders (10015919)	Conjunctival haemorrhage (10010719)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Eye pruritus (10052140)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Lacrimation increased (10023644)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.4	0.0	2.2	2	0.8	0.1	2.9
	Diarrhoea (10012735)	18	7.1	4.3	11.1	5	2.0	0.7	4.6
	Nausea (10028813)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Teething (10043183)	1	0.4	0.0	2.2	4	1.6	0.4	4.1
	Vomiting (10047700)	9	3.6	1.6	6.7	7	2.8	1.1	5.7
General disorders and administration site conditions (10018065)	Injection site bruising (10022052)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Pyrexia (10037660)	7	2.8	1.1	5.6	6	2.4	0.9	5.2
Immune system disorders (10021428)	Allergy to arthropod bite (10058285)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Milk allergy (10027633)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Infections and infestations (10021881)	Acrodermatitis (10063409)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Adenovirus infection (10060931)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Bronchiolitis (10006448)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Bronchitis (10006451)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Carbuncle (10007247)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Conjunctivitis (10010741)	1	0.4	0.0	2.2	4	1.6	0.4	4.1
	Croup infectious (10011416)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
	Ear infection (10014011)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Folliculitis (10016936)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Furuncle (10017553)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Gastroenteritis (10017888)	0	0.0	0.0	1.5	3	1.2	0.3	3.5
	Nasopharyngitis (10028810)	10	4.0	1.9	7.2	9	3.6	1.7	6.8
	Onychomycosis (10030338)	1	0.4	0.0	2.2	0	0.0	0.0	1.5

		Q-QIV N = 252				TIV-YB N = 248			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Oral candidiasis (10030963)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Otitis media (10033078)	11	4.4	2.2	7.7	14	5.6	3.1	9.3
	Otitis media acute (10033079)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Paronychia (10034016)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Pharyngitis (10034835)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Pharyngotonsillitis (10049140)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Respiratory syncytial virus infection (10061603)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
	Rhinitis (10039083)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Sinusitis (10040753)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
	Staphylococcal abscess (10041917)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Tinea infection (10060889)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Tonsillitis (10044008)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Upper respiratory tract infection (10046306)	11	4.4	2.2	7.7	11	4.4	2.2	7.8
	Viral infection (10047461)	5	2.0	0.6	4.6	6	2.4	0.9	5.2
	Viral rash (10047476)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Viral upper respiratory tract infection (10047482)	3	1.2	0.2	3.4	6	2.4	0.9	5.2
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)	0	0.0	0.0	1.5	2	0.8	0.1	2.9
	Contusion (10050584)	1	0.4	0.0	2.2	2	0.8	0.1	2.9
	Foreign body (10070245)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Head injury (10019196)	0	0.0	0.0	1.5	2	0.8	0.1	2.9
	Laceration (10023572)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Investigations (10022891)	Cardiac murmur (10007586)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	2	0.8	0.1	2.8	0	0.0	0.0	1.5
	Lactose intolerance (10023681)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Musculoskeletal and connective tissue disorders (10028395)	Muscular weakness (10028372)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Nervous system disorders (10029205)	Dizziness (10013573)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Self-induced vomiting (10048636)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Sleep terror (10041010)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Tic (10043833)	1	0.4	0.0	2.2	0	0.0	0.0	1.5

		Q-QIV N = 252				TIV-YB N = 248			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Bronchial hyperreactivity (10066091)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
	Cough (10011224)	15	6.0	3.4	9.6	14	5.6	3.1	9.3
	Nasal congestion (10028735)	7	2.8	1.1	5.6	4	1.6	0.4	4.1
	Oropharyngeal pain (10068319)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Rhinorrhoea (10039101)	15	6.0	3.4	9.6	14	5.6	3.1	9.3
	Sneezing (10041232)	3	1.2	0.2	3.4	5	2.0	0.7	4.6
	Wheezing (10047924)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Skin and subcutaneous tissue disorders (10040785)	Acne (10000496)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Dermatitis (10012431)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Dermatitis diaper (10012444)	2	0.8	0.1	2.8	3	1.2	0.3	3.5
	Dry skin (10013786)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Eczema (10014184)	2	0.8	0.1	2.8	0	0.0	0.0	1.5
	Hyperhidrosis (10020642)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Rash (10037844)	3	1.2	0.2	3.4	2	0.8	0.1	2.9
	Rash macular (10037867)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Skin lesion (10040882)	1	0.4	0.0	2.2	0	0.0	0.0	1.5

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 80 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		12	7.6	4.0	12.9	12	7.7	4.0	13.1
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	3	1.9	0.4	5.4	1	0.6	0.0	3.5
	Vomiting (10047700)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	0	0.0	0.0	2.3	2	1.3	0.2	4.6
Immune system disorders (10021428)	Allergy to arthropod bite (10058285)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Infections and infestations (10021881)	Croup infectious (10011416)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Ear infection (10014011)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Gastroenteritis (10017888)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Nasopharyngitis (10028810)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Otitis media (10033078)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Respiratory syncytial virus infection (10061603)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
	Rhinitis (10039083)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Sinusitis (10040753)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Tonsillitis (10044008)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Upper respiratory tract infection (10046306)	1	0.6	0.0	3.5	2	1.3	0.2	4.6
	Viral infection (10047461)	3	1.9	0.4	5.4	0	0.0	0.0	2.3
	Viral rash (10047476)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Laceration (10023572)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Nervous system disorders (10029205)	Dizziness (10013573)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Rash (10037844)	1	0.6	0.0	3.5	0	0.0	0.0	2.3

Q-QIV = Flu Q-QIV Vaccine; TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose; n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 81 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 252				TIV-YB N = 248			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		12	4.8	2.5	8.2	13	5.2	2.8	8.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	3	1.2	0.2	3.4	1	0.4	0.0	2.2
	Vomiting (10047700)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	0	0.0	0.0	1.5	2	0.8	0.1	2.9
Immune system disorders (10021428)	Allergy to arthropod bite (10058285)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Infections and infestations (10021881)	Croup infectious (10011416)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Ear infection (10014011)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Gastroenteritis (10017888)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Nasopharyngitis (10028810)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Otitis media (10033078)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Respiratory syncytial virus infection (10061603)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
	Rhinitis (10039083)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Sinusitis (10040753)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Tonsillitis (10044008)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Upper respiratory tract infection (10046306)	1	0.4	0.0	2.2	2	0.8	0.1	2.9
	Viral infection (10047461)	3	1.2	0.2	3.4	0	0.0	0.0	1.5
	Viral rash (10047476)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Laceration (10023572)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Nervous system disorders (10029205)	Dizziness (10013573)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Skin and subcutaneous tissue disorders (10040785)	Dermatitis diaper (10012444)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Rash (10037844)	1	0.4	0.0	2.2	0	0.0	0.0	1.5

Q-QIV = Flu Q-QIV Vaccine; TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 82 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		11	7.0	3.5	12.1	7	4.5	1.8	9.0
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	4	2.5	0.7	6.4	0	0.0	0.0	2.3
	Vomiting (10047700)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
General disorders and administration site conditions (10018065)	Injection site bruising (10022052)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Infections and infestations (10021881)	Nasopharyngitis (10028810)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Upper respiratory tract infection (10046306)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Viral infection (10047461)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
Injury, poisoning and procedural complications (10022117)	Contusion (10050584)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Musculoskeletal and connective tissue disorders (10028395)	Muscular weakness (10028372)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Cough (10011224)	2	1.3	0.2	4.5	1	0.6	0.0	3.5
	Nasal congestion (10028735)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Rhinorrhoea (10039101)	3	1.9	0.4	5.4	0	0.0	0.0	2.3
	Sneezing (10041232)	1	0.6	0.0	3.5	1	0.6	0.0	3.5
Skin and subcutaneous tissue disorders (10040785)	Hyperhidrosis (10020642)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
	Rash (10037844)	0	0.0	0.0	2.3	1	0.6	0.0	3.5

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 83 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 252				TIV-YB N = 248			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		13	5.2	2.8	8.7	7	2.8	1.1	5.7
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	5	2.0	0.6	4.6	0	0.0	0.0	1.5
	Vomiting (10047700)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
General disorders and administration site conditions (10018065)	Injection site bruising (10022052)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Infections and infestations (10021881)	Nasopharyngitis (10028810)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Upper respiratory tract infection (10046306)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Viral infection (10047461)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
Injury, poisoning and procedural complications (10022117)	Contusion (10050584)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Musculoskeletal and connective tissue disorders (10028395)	Muscular weakness (10028372)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Cough (10011224)	2	0.8	0.1	2.8	1	0.4	0.0	2.2
	Nasal congestion (10028735)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Rhinorrhoea (10039101)	4	1.6	0.4	4.0	0	0.0	0.0	1.5
	Sneezing (10041232)	1	0.4	0.0	2.2	1	0.4	0.0	2.2
Skin and subcutaneous tissue disorders (10040785)	Hyperhidrosis (10020642)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
	Rash (10037844)	0	0.0	0.0	1.5	1	0.4	0.0	2.2

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 84 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 158				TIV-YB N = 156			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		2	1.3	0.2	4.5	1	0.6	0.0	3.5
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.6	0.0	3.5	0	0.0	0.0	2.3
Infections and infestations (10021881)	Nasopharyngitis (10028810)	0	0.0	0.0	2.3	1	0.6	0.0	3.5
	Upper respiratory tract infection (10046306)	1	0.6	0.0	3.5	0	0.0	0.0	2.3

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 85 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 252				TIV-YB N = 248			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		2	0.8	0.1	2.8	1	0.4	0.0	2.2
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.4	0.0	2.2	0	0.0	0.0	1.5
Infections and infestations (10021881)	Nasopharyngitis (10028810)	0	0.0	0.0	1.5	1	0.4	0.0	2.2
	Upper respiratory tract infection (10046306)	1	0.4	0.0	2.2	0	0.0	0.0	1.5

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 86 Incidence of concomitant medication use during the 28-day (Days 0-27) post-vaccination period by dose and overall (Total vaccinated cohort)

	Q-QIV					TIV-YB				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	158	57	36.1	28.6	44.1	156	61	39.1	31.4	47.2
Any antipyretic	158	41	25.9	19.3	33.5	156	37	23.7	17.3	31.2
Prophylactic antipyretic	158	7	4.4	1.8	8.9	156	5	3.2	1.0	7.3
Any antibiotic	158	14	8.9	4.9	14.4	156	17	10.9	6.5	16.9
Prophylactic antibiotic	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
Dose 2										
Any	94	27	28.7	19.9	39.0	92	30	32.6	23.2	43.2
Any antipyretic	94	17	18.1	10.9	27.4	92	21	22.8	14.7	32.8
Prophylactic antipyretic	94	1	1.1	0.0	5.8	92	4	4.3	1.2	10.8
Any antibiotic	94	7	7.4	3.0	14.7	92	13	14.1	7.7	23.0
Prophylactic antibiotic	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Overall/dose										
Any	252	84	33.3	27.5	39.5	248	91	36.7	30.7	43.0
Any antipyretic	252	58	23.0	18.0	28.7	248	58	23.4	18.3	29.2
Prophylactic antipyretic	252	8	3.2	1.4	6.2	248	9	3.6	1.7	6.8
Any antibiotic	252	21	8.3	5.2	12.5	248	30	12.1	8.3	16.8
Prophylactic antibiotic	252	0	0.0	0.0	1.5	248	0	0.0	0.0	1.5
Overall/subject										
Any	158	73	46.2	38.2	54.3	156	74	47.4	39.4	55.6
Any antipyretic	158	51	32.3	25.1	40.2	156	51	32.7	25.4	40.7
Prophylactic antipyretic	158	7	4.4	1.8	8.9	156	6	3.8	1.4	8.2
Any antibiotic	158	21	13.3	8.4	19.6	156	27	17.3	11.7	24.2
Prophylactic antibiotic	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N = number of administered doses
n/% = number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 87 Incidence of concomitant medication use during the entire study period by dose and overall (Total vaccinated cohort)

	Q-QIV					TIV-YB				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	158	61	38.6	31.0	46.7	156	71	45.5	37.5	53.7
Any antipyretic	158	42	26.6	19.9	34.2	156	42	26.9	20.1	34.6
Prophylactic antipyretic	158	7	4.4	1.8	8.9	156	5	3.2	1.0	7.3
Any antibiotic	158	19	12.0	7.4	18.1	156	24	15.4	10.1	22.0
Prophylactic antibiotic	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
Dose 2										
Any	94	37	39.4	29.4	50.0	92	47	51.1	40.4	61.7
Any antipyretic	94	18	19.1	11.8	28.6	92	33	35.9	26.1	46.5
Prophylactic antipyretic	94	1	1.1	0.0	5.8	92	4	4.3	1.2	10.8
Any antibiotic	94	19	20.2	12.6	29.8	92	27	29.3	20.3	39.8
Prophylactic antibiotic	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Overall/dose										
Any	252	98	38.9	32.8	45.2	248	118	47.6	41.2	54.0
Any antipyretic	252	60	23.8	18.7	29.6	248	75	30.2	24.6	36.4
Prophylactic antipyretic	252	8	3.2	1.4	6.2	248	9	3.6	1.7	6.8
Any antibiotic	252	38	15.1	10.9	20.1	248	51	20.6	15.7	26.1
Prophylactic antibiotic	252	0	0.0	0.0	1.5	248	0	0.0	0.0	1.5
Overall/subject										
Any	158	81	51.3	43.2	59.3	156	89	57.1	48.9	64.9
Any antipyretic	158	52	32.9	25.7	40.8	156	61	39.1	31.4	47.2
Prophylactic antipyretic	158	7	4.4	1.8	8.9	156	6	3.8	1.4	8.2
Any antibiotic	158	35	22.2	15.9	29.4	156	46	29.5	22.5	37.3
Prophylactic antibiotic	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
For each dose and overall/subject:
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N = number of administered doses
n/% = number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 88 Overall number and percentage of subjects who received concomitant vaccination (Total vaccinated cohort)

	Q-QIV					TIV-YB				
				95% CI					95% CI	
Concomitant vaccination	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1										
DTaP	158	17	10.8	6.4	16.7	156	14	9.0	5.0	14.6
DTaP/Hep B/IPV	158	6	3.8	1.4	8.1	156	6	3.8	1.4	8.2
DTaP/Hep B/IPV, HiB, PCV	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Hep A	158	31	19.6	13.7	26.7	156	23	14.7	9.6	21.3
Hep B	158	13	8.2	4.5	13.7	156	9	5.8	2.7	10.7
Hib	158	19	12.0	7.4	18.1	156	17	10.9	6.5	16.9
IPV	158	16	10.1	5.9	15.9	156	12	7.7	4.0	13.1
Influenza	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
MMR	158	15	9.5	5.4	15.2	156	9	5.8	2.7	10.7
MMRV	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
PCV	158	21	13.3	8.4	19.6	156	20	12.8	8.0	19.1
Pneumococcal	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Polio	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Rotavirus	158	11	7.0	3.5	12.1	156	11	7.1	3.6	12.3
Varicella	158	14	8.9	4.9	14.4	156	9	5.8	2.7	10.7
Dose 2										
DTaP	94	12	12.8	6.8	21.2	92	13	14.1	7.7	23.0
DTaP/Hep B/IPV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
DTaP/Hep B/IPV, HiB, PCV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Hep A	94	19	20.2	12.6	29.8	92	20	21.7	13.8	31.6
Hep B	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Hib	94	16	17.0	10.1	26.2	92	13	14.1	7.7	23.0
IPV	94	2	2.1	0.3	7.5	92	7	7.6	3.1	15.1
Influenza	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
MMR	94	12	12.8	6.8	21.2	92	15	16.3	9.4	25.5
MMRV	94	1	1.1	0.0	5.8	92	1	1.1	0.0	5.9
PCV	94	14	14.9	8.4	23.7	92	9	9.8	4.6	17.8
Pneumococcal	94	2	2.1	0.3	7.5	92	0	0.0	0.0	3.9
Polio	94	2	2.1	0.3	7.5	92	2	2.2	0.3	7.6
Rotavirus	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Varicella	94	11	11.7	6.0	20.0	92	14	15.2	8.6	24.2
Overall/dose										
DTaP	252	29	11.5	7.8	16.1	248	27	10.9	7.3	15.4
DTaP/Hep B/IPV	252	6	2.4	0.9	5.1	248	6	2.4	0.9	5.2
DTaP/Hep B/IPV, HiB, PCV	252	0	0.0	0.0	1.5	248	1	0.4	0.0	2.2
Hep A	252	50	19.8	15.1	25.3	248	43	17.3	12.8	22.6
Hep B	252	13	5.2	2.8	8.7	248	9	3.6	1.7	6.8
Hib	252	35	13.9	9.9	18.8	248	30	12.1	8.3	16.8
IPV	252	19	7.5	4.6	11.5	248	19	7.7	4.7	11.7
Influenza	252	0	0.0	0.0	1.5	248	1	0.4	0.0	2.2
MMR	252	27	10.7	7.2	15.2	248	24	9.7	6.3	14.1
MMRV	252	1	0.4	0.0	2.2	248	1	0.4	0.0	2.2
PCV	252	35	13.9	9.9	18.8	248	29	11.7	8.0	16.4
Pneumococcal	252	2	0.8	0.1	2.8	248	1	0.4	0.0	2.2
Polio	252	2	0.8	0.1	2.8	248	3	1.2	0.3	3.5
Rotavirus	252	11	4.4	2.2	7.7	248	11	4.4	2.2	7.8
Varicella	252	25	9.9	6.5	14.3	248	23	9.3	6.0	13.6

	Q-QIV					TIV-YB				
				95% CI					95% CI	
Concomitant vaccination	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject										
DTaP	158	29	18.4	12.7	25.3	156	26	16.7	11.2	23.5
DTaP/Hep B/IPV	158	6	3.8	1.4	8.1	156	6	3.8	1.4	8.2
DTaP/Hep B/IPV, HiB, PCV	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Hep A	158	50	31.6	24.5	39.5	156	43	27.6	20.7	35.3
Hep B	158	13	8.2	4.5	13.7	156	9	5.8	2.7	10.7
Hib	158	35	22.2	15.9	29.4	156	29	18.6	12.8	25.6
IPV	158	18	11.4	6.9	17.4	156	19	12.2	7.5	18.4
Influenza	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
MMR	158	27	17.1	11.6	23.9	156	24	15.4	10.1	22.0
MMRV	158	1	0.6	0.0	3.5	156	1	0.6	0.0	3.5
PCV	158	32	20.3	14.3	27.4	156	26	16.7	11.2	23.5
Pneumococcal	158	2	1.3	0.2	4.5	156	1	0.6	0.0	3.5
Polio	158	2	1.3	0.2	4.5	156	3	1.9	0.4	5.5
Rotavirus	158	11	7.0	3.5	12.1	156	11	7.1	3.6	12.3
Varicella	158	25	15.8	10.5	22.5	156	23	14.7	9.6	21.3

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = Fluzone Vaccine
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects with a concomitant vaccination
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses with a concomitant vaccination
95%CI = Exact 95% confidence interval: LL = lower limit, UL = upper limit

Table 89 Overall number and percentage of subjects who received concomitant vaccination within 7 days of the study vaccine(Day 0 to Day 6) (Total vaccinated cohort)

	Q-QIV					TIV-YB				
				95% CI					95% CI	
Concomitant vaccination	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
DTaP	158	15	9.5	5.4	15.2	156	10	6.4	3.1	11.5
DTaP/Hep B/IPV	158	6	3.8	1.4	8.1	156	6	3.8	1.4	8.2
DTaP/Hep B/IPV, HiB, PCV	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Hep A	158	18	11.4	6.9	17.4	156	16	10.3	6.0	16.1
Hep B	158	13	8.2	4.5	13.7	156	9	5.8	2.7	10.7
Hib	158	18	11.4	6.9	17.4	156	14	9.0	5.0	14.6
IPV	158	14	8.9	4.9	14.4	156	11	7.1	3.6	12.3
Influenza	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
MMR	158	15	9.5	5.4	15.2	156	9	5.8	2.7	10.7
MMRV	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
PCV	158	21	13.3	8.4	19.6	156	18	11.5	7.0	17.6
Pneumococcal	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Polio	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Rotavirus	158	11	7.0	3.5	12.1	156	11	7.1	3.6	12.3
Varicella	158	14	8.9	4.9	14.4	156	9	5.8	2.7	10.7
Dose 2										
DTaP	94	2	2.1	0.3	7.5	92	1	1.1	0.0	5.9
DTaP/Hep B/IPV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
DTaP/Hep B/IPV, HiB, PCV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Hep A	94	5	5.3	1.7	12.0	92	1	1.1	0.0	5.9
Hep B	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Hib	94	2	2.1	0.3	7.5	92	3	3.3	0.7	9.2
IPV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Influenza	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
MMR	94	3	3.2	0.7	9.0	92	3	3.3	0.7	9.2
MMRV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
PCV	94	1	1.1	0.0	5.8	92	2	2.2	0.3	7.6
Pneumococcal	94	1	1.1	0.0	5.8	92	0	0.0	0.0	3.9
Polio	94	0	0.0	0.0	3.8	92	1	1.1	0.0	5.9
Rotavirus	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Varicella	94	2	2.1	0.3	7.5	92	3	3.3	0.7	9.2
Overall/dose										
DTaP	252	17	6.7	4.0	10.6	248	11	4.4	2.2	7.8
DTaP/Hep B/IPV	252	6	2.4	0.9	5.1	248	6	2.4	0.9	5.2
DTaP/Hep B/IPV, HiB, PCV	252	0	0.0	0.0	1.5	248	1	0.4	0.0	2.2
Hep A	252	23	9.1	5.9	13.4	248	17	6.9	4.0	10.7
Hep B	252	13	5.2	2.8	8.7	248	9	3.6	1.7	6.8
Hib	252	20	7.9	4.9	12.0	248	17	6.9	4.0	10.7
IPV	252	14	5.6	3.1	9.1	248	11	4.4	2.2	7.8
Influenza	252	0	0.0	0.0	1.5	248	0	0.0	0.0	1.5
MMR	252	18	7.1	4.3	11.1	248	12	4.8	2.5	8.3
MMRV	252	0	0.0	0.0	1.5	248	0	0.0	0.0	1.5
PCV	252	22	8.7	5.6	12.9	248	20	8.1	5.0	12.2
Pneumococcal	252	1	0.4	0.0	2.2	248	1	0.4	0.0	2.2
Polio	252	0	0.0	0.0	1.5	248	2	0.8	0.1	2.9
Rotavirus	252	11	4.4	2.2	7.7	248	11	4.4	2.2	7.8
Varicella	252	16	6.3	3.7	10.1	248	12	4.8	2.5	8.3

	Q-QIV					TIV-YB				
				95% CI					95% CI	
Concomitant vaccination	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject										
DTaP	158	17	10.8	6.4	16.7	156	10	6.4	3.1	11.5
DTaP/Hep B/IPV	158	6	3.8	1.4	8.1	156	6	3.8	1.4	8.2
DTaP/Hep B/IPV, HiB, PCV	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Hep A	158	23	14.6	9.5	21.0	156	17	10.9	6.5	16.9
Hep B	158	13	8.2	4.5	13.7	156	9	5.8	2.7	10.7
Hib	158	20	12.7	7.9	18.9	156	16	10.3	6.0	16.1
IPV	158	14	8.9	4.9	14.4	156	11	7.1	3.6	12.3
Influenza	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
MMR	158	18	11.4	6.9	17.4	156	12	7.7	4.0	13.1
MMRV	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
PCV	158	22	13.9	8.9	20.3	156	19	12.2	7.5	18.4
Pneumococcal	158	1	0.6	0.0	3.5	156	1	0.6	0.0	3.5
Polio	158	0	0.0	0.0	2.3	156	2	1.3	0.2	4.6
Rotavirus	158	11	7.0	3.5	12.1	156	11	7.1	3.6	12.3
Varicella	158	16	10.1	5.9	15.9	156	12	7.7	4.0	13.1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = Fluzone Vaccine
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects with a concomitant vaccination
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses with a concomitant vaccination
95%CI = Exact 95% confidence interval: LL = lower limit, UL = upper limit

Table 90 Overall number and percentage of subjects who received concomitant vaccination on the same day as the study vaccine (Total vaccinated cohort)

	Q-QIV					TIV-YB				
				95% CI					95% CI	
Concomitant vaccination	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
DTaP	158	15	9.5	5.4	15.2	156	10	6.4	3.1	11.5
DTaP/Hep B/IPV	158	6	3.8	1.4	8.1	156	6	3.8	1.4	8.2
DTaP/Hep B/IPV, HiB, PCV	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Hep A	158	18	11.4	6.9	17.4	156	16	10.3	6.0	16.1
Hep B	158	13	8.2	4.5	13.7	156	9	5.8	2.7	10.7
Hib	158	18	11.4	6.9	17.4	156	14	9.0	5.0	14.6
IPV	158	14	8.9	4.9	14.4	156	11	7.1	3.6	12.3
Influenza	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
MMR	158	14	8.9	4.9	14.4	156	9	5.8	2.7	10.7
MMRV	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
PCV	158	21	13.3	8.4	19.6	156	18	11.5	7.0	17.6
Pneumococcal	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Polio	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Rotavirus	158	11	7.0	3.5	12.1	156	11	7.1	3.6	12.3
Varicella	158	13	8.2	4.5	13.7	156	9	5.8	2.7	10.7
Dose 2										
DTaP	94	1	1.1	0.0	5.8	92	1	1.1	0.0	5.9
DTaP/Hep B/IPV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
DTaP/Hep B/IPV, HiB, PCV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Hep A	94	4	4.3	1.2	10.5	92	1	1.1	0.0	5.9
Hep B	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Hib	94	1	1.1	0.0	5.8	92	3	3.3	0.7	9.2
IPV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Influenza	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
MMR	94	2	2.1	0.3	7.5	92	3	3.3	0.7	9.2
MMRV	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
PCV	94	1	1.1	0.0	5.8	92	2	2.2	0.3	7.6
Pneumococcal	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Polio	94	0	0.0	0.0	3.8	92	1	1.1	0.0	5.9
Rotavirus	94	0	0.0	0.0	3.8	92	0	0.0	0.0	3.9
Varicella	94	2	2.1	0.3	7.5	92	3	3.3	0.7	9.2
Overall/dose										
DTaP	252	16	6.3	3.7	10.1	248	11	4.4	2.2	7.8
DTaP/Hep B/IPV	252	6	2.4	0.9	5.1	248	6	2.4	0.9	5.2
DTaP/Hep B/IPV, HiB, PCV	252	0	0.0	0.0	1.5	248	1	0.4	0.0	2.2
Hep A	252	22	8.7	5.6	12.9	248	17	6.9	4.0	10.7
Hep B	252	13	5.2	2.8	8.7	248	9	3.6	1.7	6.8
Hib	252	19	7.5	4.6	11.5	248	17	6.9	4.0	10.7
IPV	252	14	5.6	3.1	9.1	248	11	4.4	2.2	7.8
Influenza	252	0	0.0	0.0	1.5	248	0	0.0	0.0	1.5
MMR	252	16	6.3	3.7	10.1	248	12	4.8	2.5	8.3
MMRV	252	0	0.0	0.0	1.5	248	0	0.0	0.0	1.5
PCV	252	22	8.7	5.6	12.9	248	20	8.1	5.0	12.2
Pneumococcal	252	0	0.0	0.0	1.5	248	1	0.4	0.0	2.2
Polio	252	0	0.0	0.0	1.5	248	2	0.8	0.1	2.9
Rotavirus	252	11	4.4	2.2	7.7	248	11	4.4	2.2	7.8
Varicella	252	15	6.0	3.4	9.6	248	12	4.8	2.5	8.3

	Q-QIV					TIV-YB				
				95% CI					95% CI	
Concomitant vaccination	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Overall/subject										
DTaP	158	16	10.1	5.9	15.9	156	10	6.4	3.1	11.5
DTaP/Hep B/IPV	158	6	3.8	1.4	8.1	156	6	3.8	1.4	8.2
DTaP/Hep B/IPV, HiB, PCV	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Hep A	158	22	13.9	8.9	20.3	156	17	10.9	6.5	16.9
Hep B	158	13	8.2	4.5	13.7	156	9	5.8	2.7	10.7
Hib	158	19	12.0	7.4	18.1	156	16	10.3	6.0	16.1
IPV	158	14	8.9	4.9	14.4	156	11	7.1	3.6	12.3
Influenza	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
MMR	158	16	10.1	5.9	15.9	156	12	7.7	4.0	13.1
MMRV	158	0	0.0	0.0	2.3	156	0	0.0	0.0	2.3
PCV	158	22	13.9	8.9	20.3	156	19	12.2	7.5	18.4
Pneumococcal	158	0	0.0	0.0	2.3	156	1	0.6	0.0	3.5
Polio	158	0	0.0	0.0	2.3	156	2	1.3	0.2	4.6
Rotavirus	158	11	7.0	3.5	12.1	156	11	7.1	3.6	12.3
Varicella	158	15	9.5	5.4	15.2	156	12	7.7	4.0	13.1

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = Fluzone Vaccine
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects with a concomitant vaccination
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses with a concomitant vaccination
95%CI = Exact 95% confidence interval: LL = lower limit, UL = upper limit

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12. STUDY REPORT AUTHORS /CONTRIBUTING AUTHORS

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13. SERIOUS ADVERSE EVENTS / OTHER SIGNIFICANT ADVERSE EVENTS / PREGNANCY

13.1. SAE Listing(s)

Table 91 Listing of SAEs reported during the entire study period (Total vaccinated cohort)

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
Q-QIV	(b) (6)	NA	34	M	Dehydration	Dehydration	Metabolism and nutrition disorders	HO	1	145	9	3	N	Recovered/resolved
		NA	10	M	Obstructive sleep apnea	Sleep apnoea syndrome	Respiratory, thoracic and mediastinal disorders	HO	2	99	.	3	N	Not recovered/not resolved
		NA	7	F	Viral illness	Viral infection	Infections and infestations	HO	1	24	4	3	N	Recovered/resolved
		NA	27	F	Respiratory syncytial viral illness	Respiratory syncytial virus infection	Infections and infestations	HO	2	21	9	3	N	Recovered/resolved
		NA	18	F	Respiratory syncytial virus	Respiratory syncytial virus infection	Infections and infestations	HO	2	28	11	3	N	Recovered/resolved
TIV-YB		NA	10	M	Suspected seizure activity	Convulsion	Nervous system disorders	HO	2	70	.	3	N	Not recovered/not resolved
		NA	14	M	Hospitalization for failure to thrive	Failure to thrive	Metabolism and nutrition disorders	HO	2	144	.	2	N	Recovering/resolving
		NA	10	F	Respiratory syncytial virus bronchiolitis	Respiratory syncytial virus bronchiolitis	Infections and infestations	HO	2	16	9	3	N	Recovered/resolved
		NA	14	M	Right sided neck abscess	Abscess neck	Infections and infestations	HO	2	107	5	1	N	Recovered/resolved

Q-QIV = Flu Q-QIV Vaccine
TIV-YB = *Fluzone* Vaccine
NA = Not Applicable (SAEs available only in Clinical Data)
MED = Medically attended visit

13.2. Clinical Narratives for SAEs

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Unblinded Report – With Suspect Products and Serious Events

Study Number: 200806

Study Center ID: 204456

Subject ID: (b) (6)

Randomization Number:

Case ID: (b) (6)

Suspect Products: Fluzone

Serious Events: Convulsion

Narrative: This 10-month-old male subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6), for prophylaxis.

Concurrent medical conditions included macrocephaly and cafe au lait spots.

On (b) (6) 20:20, 70 days after receiving Flu Q-QIV vs Fluzone the subject developed severe - grade 3 seizure. Serious criteria included hospitalization and GSK medically significant. The outcome of seizure was unresolved.

The investigator considered that there was no reasonable possibility that the seizure may have been caused by Flu Q-QIV vs Fluzone.

Relevant Tests: Lab Tests: EEG performed on (b) (6) - no epileptiform activity noted.
CT performed on (b) (6) - No acute intracranial hemorrhageor mass effect, prominence of ventricles and extra-axial spaces - suggestive of beggining enlargement of subarachnoid spaces, extensive paranasal sinus opacification.
MRI of brain and orbits, face and neck performed on (b) (6) - no abnormal intracranial signal or mass effect, prominence of extra axial spaces may represent benign enlargement of subarachnoid spaces, paranasal sinus mucosal disease.

Investigator comments : On (b) (6), mom contacted PMD at 2034, stating that subject had just had an episode where he seized up and became stiff for about 2-3 minutes and then became limp and unresponsive for about 5 minutes. Subject continue to breathe shallowly, did not urinte and did not have a fever either during or prior to the event. After 5 minutes, subject awoke but was drowsy and would not use his hands for about 3 minutes. PMD advised mom take him to ED for evaluation. Mom arrived at ED and subject was evaluated by a neurologist to evaluate for seizure. CT of brain was performed in the ED and showed no intracranial bleed but did note prominence of ventricles and extra-axial spaces. Neurology recommended an MRI and EEG and the subject was admitted for observation while those tests could be arranged. An EEG was performed while admitted and read as normal. An MRI was performed while under sedation and was found to be normal with the exception of the prominence of the ventricles and the extra axial spaces. No further seizures were noted while hospitalized and the subject was dicharged from the hospital on (b) (6). Baby was brought by ambulance to Emergency department (ED) on (b) (6) as mom reported that evening that the subject had an episode where he put his arms out

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and they were shaking and he had a blank stare that lasted for about 10 minutes. Upon exam in the ED, the subject was found to be in his normal state of health and at his baseline. Neurology was consulted and since he had been hospitalized and evaluated previously, they recommended an outpatient EEG be performed. The subject was discharged from the ED after several hours. Mom currently reports that subject has had 2 other episodes of seizure like activity but that she has not brought him to the ED as he seems to be ok when he comes out and they have not been as long. Outpatient EEG was obtained on (b) (6), but report is not yet available. No medications have been prescribed to this point.
There is no family history of seizures, however, the subject has macrocephaly and cafe-au-lait spots on his body. Cafe-au-lait spots can be highly indictative of neurofibromatosis which is known to cause seizure activity. PI deems this not related to the study product as the subject had received his last study vaccine more than 60 days prior to the event and because he has significant other history to explain and more plausible cause to this event (Macrocephaly and cafe-au-lait spots). (b) (6) - Subject was seen by Neurosurgeon regarding macrocephaly on (b) (6). It was determined that macrocephaly was benign and not contributing to his seizures. He was seen in the ED on (b) (6) for another seizure reported at home. He was given a script for Lorazepam (2mg/ml) 0.5ml if he has seizure lasting longer than 3 minitues or more than 3 in one hour. He was seen for a clinic visit on (b) (6), as he had another seizure in
daycare. Mom states that he has had several seizures at home that she did not seek medical attention for. It is not clear if she needed to administer lorazepam or not. There is concern that the seizures may occur due to illness or when child is tired. A sleep deprived EEG is being ordered at this time, but is not yet scheduled.

Study Number: 200806

Study Center ID: 204456

Subject ID: (b) (6)

Randomization Number:

Case ID: (b) (6)

Suspect Products: Fluzone

Serious Events: Failure to thrive

Narrative: This 12-month-old male subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6), for prophylaxis.

On (b) (6) 14:46, 144 days after receiving Flu Q-QIV vs Fluzone the subject developed moderate - grade 2 failure to thrive. Serious criteria included hospitalization and GSK medically significant. The outcome of failure to thrive was recovering/resolving.

The investigator considered that there was no reasonable possibility that the failure to thrive may have been caused by Flu Q-QIV vs Fluzone.

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Relevant Tests: Lab Tests: Endoscopy - showed esophageal inflammation consistent with Eosinophilic esophagitis.

Investigator comments : The subject has had a long history of issues with failure to thrive. Frequent weight check visits have been performed over the course of the study (and prior to that) and his weight would increase when outside services were involved but then decrease when the services seemed no longer rendered due to improvment. The mother insisted that the issues were related to chronic vomitting and failure to eat what was placed infront of him. Different treatments for GERD were tried and were ultimately discontinued as mom reported that there was no improvement. After recent issues with a decrease in the subjects weight, it was decided to admit him to the hospital to have some endoscopic tests to see if there was something else wrong with his uppper gastrointestinal system and to see if under a controlled environment, would the child thrive. The child was admitted on (b) (6) . Weight increase was evident from the beginning but there still appeared to be an issue with some vomitting and coughing when eating and shortly thereafter. An endoscopy was performed and he was found to have eosinophilic esophagitis. This was not felt to be a contributing factor in his failure to thrive as he had shown weight increase at several different time prior to the hospitalization and during the hopsitalization, prior to the discovery of the eosinophilic esophagitis. It was felt that nutritional neglect was the cause of the failure to thrive. As a result the subject was placed with a foster family by Child protective services. He was discharged to the foster family with prescriptions for Pulmicort, Prevacid and Elacare Junior on (b) (6)

Study Number: 200806

Study Center ID: 204456

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Dehydration

Narrative: This 2-year-old male subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6) , for prophylaxis.

Concurrent medical conditions included constipation.

On (b) (6) 08:14, 145 days after receiving Flu Q-QIV vs Fluzone the subject developed severe - grade 3 dehydration. Serious criteria included hospitalization. The subject was treated with glucose + sodium chloride (Dextrose 5% In Normal Saline), Mineral Oil Retention Enema, ondansetron, ondansetron, electrolytes nos + macrogol (Golytely) and fleet enema (nos) (Fleet Enema). The outcome of dehydration was resolved on 4th May 2014 14:15.

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The investigator considered that there was no reasonable possibility that the dehydration may have been caused by Flu Q-QIV vs Fluzone.

Investigator comments : Subject was brought to the emergency department on (b) (6) by mother for complaint of 5 days of vomiting initially starting only after he ate solid food and pregressing to whenever he would drink as well. Mom also had a complaint of 2 weeks without having a stool and only 2 instances of urination within 24 hours of the ED admission. Mom reported that child complained that his stomach hurt. Abdominal x-ray revealed a large amount of stool in the rectum, descending and sigmoid colon. A fleets enema was given in the ED and the child had 3 stools. Oral rehydration was attemped in the ED but was unsuccessful as the child continued to vomit. It was decided to start an IV and admit the child for further hydration and evaluation by the GI service as the child was so significantly consitpated. Once admitted, child was given a mineral oil enema and was rechallanged with oral fluids. Once the child was able to tolerate orally, golytely was administered to push out any remaining stool that could not be reached with the enema. He was placed on Miralax and Senokot and monitored for a coupl of days to be sure that these medications would keep his bowels running. When it was proven that these were working well, the child was discharged to home with mom.

Study Number: 200806

Study Center ID: 204456

Subject ID: (b) (6)

Randomization Number:

Case ID (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Sleep apnoea syndrome

Narrative: This 10-month-old male subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6), for prophylaxis.

On (b) (6) 04:37, 99 days after receiving Flu Q-QIV vs Fluzone the subject developed severe - grade 3 obstructive sleep apnea syndrome. Serious criteria included hospitalization. The outcome of obstructive sleep apnea syndrome was unresolved.

The investigator considered that there was no reasonable possibility that the obstructive sleep apnea syndrome may have been caused by Flu Q-QIV vs Fluzone.

Relevant Tests: Lab Tests: Sleep study performed on (b) (6) revealed severe chronic obstructive sleep apnea.

Investigator comments : Mom had long reported a history in the subject that he would snore loudly at night and if he was not snoring he would have very loud breathing. He was referred to the Pulmonary Clinic

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where a sleep study was ordered. He was found to have severe obstructive Sleep apnea and laryngomalacia and his oxygen saturation dropped down to as low as 75%. Given this information, it was deciced to have ENT service admit him for rigid bronchoscope and potential surgical intervention based upon other finding noted on direct observation. The subject was adminted on (b) (6) and monitored with a cardiac/apnea monitor until surgery was scheduled for (b) (6) . During the bronchoscopy, it was found that the subject also had adenoid hypertrophy. An adnoidectomy and a supraglottoplasty procedure was performed. He was observed postoperatively for a couple of days and was found to recooperate from the surgery well. He was discharged on (b) (6) . Mom reports at this time that he is still dealing with obstructive sleep apnea and a sleep study performed on (b) (6) still shows the sleep apnea. Mom states she is awaiting insurance approval of CPAP at this time.

Study Number: 200806

Study Center ID: 204457

Subject ID: (b) (6)

Randomization Number:

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Viral infection

Narrative: This 7-month-old female subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6) , for prophylaxis.

On (b) (6) , 24 days after receiving Flu Q-QIV vs Fluzone the subject developed severe - grade 3 viral infection. Serious criteria included hospitalization. The subject was treated with ibuprofen and ceftriaxone (Rocephin). The outcome of viral infection was resolved on 8th January 2014.

The investigator considered that there was no reasonable possibility that the viral infection may have been caused by Flu Q-QIV vs Fluzone.

Relevant Tests: Lab Tests: (b) (6) : Influenza A and B antigen both negative. Urinalysis normal. Urine culture negative.
(b) (6) : Chest X ray: Peribronchial thickening which is nonspecific but is most often seen with viral infection or reactive airways disease.
Diagnostic results (unless otherwise stated, normal values were not provided): On (b) (6) , Body temperature result was 38.3 Celcius (normal low: 36.11, normal high: 37.94). On (b) (6) , Band Neutrophil count result was 22 % (normal low: 5, normal high: 11), C-reactive protein result was 5.04 mg/dl (normal low: 0.01, normal high: 0.28), Hematocrit result was 31.1 % (normal low: 33, normal high: 38), Lymphocytes result was 34 % (normal low: 45, normal high: 76), Mean corpuscular volume result was 85.0 fl (normal low: 70, normal high: 84), Monocytes result was 9 % (normal low: 3, normal high: 6), Red blood cell count result was 3.66 10E12/L (normal low: 3.7, normal high: 4.9) and White blood cell count

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result was 16.6 610E9/L (normal low: 6, normal high: 17).

Investigator comments : (b) (6) Subject evaluated at local emergency room for fever where subject had a catheterized urine collected for analysis and culture as well as a nasopharyngeal swab for Influenza A and B. Temperature at this visit was 38.3 degrees Celsius. All results normal with culture pending. Subject discharged. (b) (6) Subject taken to a different emergency room due to continued fever of 40 degrees Celsius. Subject had complete blood count, blood culture, C reactive protein as well as a chest x ray and was admitted for observation and treated with intravenous Rocephin pending cultures. (b) (6) Urine culture final result is negative. (b) (6) Subject discharged as resolved and in stable condition.

Study Number: 200806

Study Center ID: 204463

Subject ID: (b) (6)

Randomization Number:

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Respiratory syncytial virus infection

Narrative: This 2-year-old female subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 21 days after receiving Flu Q-QIV vs Fluzone the subject developed severe - grade 3 respiratory syncytial virus infection. Serious criteria included hospitalization. The subject was treated with ibuprofen (Children'S Motrin) and intravenous fluid (nos) (Intravenous Fluids). The outcome of respiratory syncytial virus infection was recovered/resolved on 2nd January 2014.

The investigator considered that there was no reasonable possibility that the respiratory syncytial virus infection may have been caused by Flu Q-QIV vs Fluzone.

Relevant Tests: Lab Tests: Influenza A rapid and Influenza B rapid test were both negative. Respiratory Syncytial Virus test was positive.

Investigator comments : (b) (6) subject came in with mother for Visit 2 Day 56 visit. Subject's mother stated subject had been seen in the ER for virus and that her sibling in the same study was admitted into the hospital for being positive for Respiratory Syncytial Viral Illness. Mother stated subject was not admitted to the hospital and was only seen and treated for a virus by the ER and then released with no scripts. Recieved prgress notes from the visit and it has been confirmed that the subject was also admitted into the hospital for Respiratory Syncytical Viral Illness and also treated for left otitis media. Subject was seen and evaluated by a Sub-I on (b) (6) and the exam was found to be normal.

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Subject was treated during hospital stay with Intravenous fluids for hydration and Invtravenouse ceftriaxone for the left otitis media (AE). Influenza A rapid and Influenza B rapid test were both negative. Respiratory Syncytial Virus test was positive.

Study Number: 200806

Study Center ID: 204463

Subject ID: (b) (6)

Randomization Number:

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Respiratory syncytial virus infection

Narrative: This 18-month-old female subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6), for prophylaxis.

Concurrent medical conditions included reactive airways disease and lung disorder.

On (b) (6), 28 days after receiving Flu Q-QIV vs Fluzone the subject developed severe - grade 3 respiratory syncytial virus infection. Serious criteria included hospitalization. The subject was treated with cefdinir (Omnicef), prednisolone and salbutamol (Albuterol). The outcome of respiratory syncytial virus infection was recovered/resolved on 11th January 2014.

The investigator considered that there was no reasonable possibility that the respiratory syncytial virus infection may have been caused by Flu Q-QIV vs Fluzone. Relevant Tests: Lab Tests: Positive RSV test (b) (6)

Investigator comments : Guardian returned to the office today with subjects sibling and reported subject was admitted to the hospital on (b) (6) testing postivie for RSV. Medical records have been requested- medications are not known at this time other than IV fluids and antibiotics have been started but names not known.
Spoke with Guardian on (b) (6) and subject is being released from the hospital this AM to go home. Subject has been fever free since 02Jan2014. Guardian is not sure what medications subject received in the hospital just knows she got IV antibiotics. Medical records have not been received.
Spoke with Guardian and captured end date for RSV and end dates for Medications used to treat RSV. Guardian disclosed that subject is still taking Albuterol to treat asthma. When questioned, guardian disclosed subject has had asthma since she was 8 months old and has been on Albuterol treatment for this condition since diagnosis. Guardian was re-educated that she should have disclosed this at Visit 1 for subject's safety. She said she understood and will be sure to disclose all medical history in the future. Medical histroy has been updated and Albuterol added as medication for treatment of Asthma.
(b) (6) Medical Records for ER visit on (b) (6) were received and reviewed. Subject was not

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admitted to the hospital on (b) (6) but reported with cough and fever, subject was tested for RSV and Influenza and both were negative. Subject was diagnosed with Acute Upper Respiratory Infection and Exacerbation of Reactive Airway Disease. Both have been recorded as AEs. Hospital was contacted and questioned if subject was infact hospitalized and treated for RSV. Hospital Medical Records department confirmed subject was admitted on (b) (6) but did not confirm reason for hospitalization, the admission and hospitalization records have been requested but not received. At this time, SAE will stay Respiratory Syncytial Virus as per the guardian's verbal report. Medical history of asthma has also been revised to Reactive Airway Disease and additional medical history of premature lungs, 26 Week Preemie and Sleep Apnea have been added to medical history.

Study Number: 200806

Study Center ID: 204464

Subject ID: (b) (6)

Randomization Number:

Case ID: (b) (6)

Suspect Products: Fluzone

Serious Events: Abscess neck

Narrative: This 14-month-old male subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 107 days after receiving Flu Q-QIV vs Fluzone the subject developed mild - grade 1 abscess neck. Serious criteria included hospitalization. The subject was treated with amoxicillin + clavulanate potassium (Amoxicillin + Clavulanate K), glucose + potassium chloride + sodium chloride (Dextrose + Potassium Chloride + Sodium Chloride), ampicillin + sulbactam (Ampicillin (Sulbactam)), paracetamol (Acetaminophen), ibuprofen and lidocaine. The outcome of abscess neck was recovered/resolved on 17th March 2014.

The investigator considered that there was no reasonable possibility that the abscess neck may have been caused by Flu Q-QIV vs Fluzone.

Investigator comments : (b) (6) : PATIENT CAME INTO OFFICE AND WAS ASSESSED BY PROVIDER- DIAGNOSED WITH SWELLING IN HEAD AND NECK (MOM HAD NOTICED LUMP ON SIDE OF NECK 13MAR2014- THOUGHT HAD BUMPED AT DAYCARE, MOM CONFIRMED 14MAR2014- THEY DID NOT BUMP IT AT DAYCARE, PATIENT WOKE UP (b) (6) - WITH RED BUMP SWOLLEN- CAME INTO OFFICE THAT SAME DAY) PATIENT WAS REFERRED TO ENT. (b) (6) - PATIENT WENT TO ENT COULD NOT BE SEEN- WAS SENT TO CHILDREN'S HOSPITAL - ULTRASOUND DONE- SURGERY WAS DONE THAT DAY (b) (6) TO DRAIN RIGHT SIDED NECK ABSCESS. PATIENT WAS KEPT IN HOPSITAL OVERNIGHT UNTIL (b) (6) WHEN HE WAS DISCHARGED

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(b) (6) - PATIENT CAME INTO OFFICE TO FOLLOW UP FROM HOSPITALIZATION.

Study Number: 200806

Study Center ID:

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone

Serious Events: Respiratory syncytial virus bronchiolitis

Narrative: This 10-month-old female subject was enrolled in a blinded study titled A Phase II, observer-blind, randomised, controlled, multi-centre study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's trivalent influenza vaccine Fluzone®, administered intramuscularly to children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included asthma, ventricular septal defect, premature birth, foramen ovale patent and reactive airways disease.

On (b) (6) 21:32, 16 days after receiving Flu Q-QIV vs Fluzone the subject developed severe - grade 3 respiratory syncytial virus bronchiolitis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with salbutamol (Albuterol), paracetamol (Acetaminophen), ampicillin, ibuprofen and ipratropium bromide, salbutamol sulfate (Duoneb). The outcome of respiratory syncytial virus bronchiolitis was recovered/resolved on (b) (6).

The investigator considered that there was no reasonable possibility that the respiratory syncytial virus bronchiolitis may have been caused by Flu Q-QIV vs Fluzone.

Relevant Tests: CHEST X-RAY. TEST DATE: (b) (6). IMPRESSION: Changes of small airways disease. Diagnostic considerations include reactive airway disease versus inflammatory etiologies. Lab Results (b) (6): INFLUENZA A: Negative; INFLUENZA B: Negative; RSV, SUBTYPE A: Positive; RSV, SUBTYPE B: Negative; PARAINFLUENZA 1: Negative; PARAINFLUENZA 2: Negative; PARAINFLUENZA 3: Negative; RHINOVIRUS: Negative; HUMAN METAPNEUMOVIRUS: Negative; ADENOVIRUS: Positive.

Investigator comments : Subject's mother contacted site on Jan 27th 2014 at 15:01. Informed site staff that subject was taken to ER on (b) (6) Initial impression was deemed as Shortness of Breath. Subject was admitted to hospital on (b) (6) and is undergoing further diagnostics.
Per Methodist Hospital Records, subject was taken to the ER on (b) (6) at 18:24 presenting shortness of breath. Subject was treated with nebulizer and steroids. Initial impression was Acute Bronchiolitis, Infant Respiratory distress Syndrome and Upper Respiratory Infection. Subject was diagnosed with upper respiratory infection and discharged on (b) (6) at 21:56
Per UC Davis medical records, subject was taken to the ER on (b) (6) presenting cough x 5 days,

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fevers (up to 101 rectal) x 4 days. Subject was given medications and a chest x-ray was performed. Lab tests were conducted which resulted in Positive for RSV, Subtype A and Positive result for Adenovirus. Discharge summary states that subject status improved and subject was discharged on (b) (6)
RSV+ bronchiolitis at unspecified time after vaccination. Cause of condition is RSV virus, not vaccination, and is common in this age range.

GlaxoSmithKline Biologicals, SA

Study detailed title

A Phase III, observer-blind, randomized, controlled, multi-center study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's quadrivalent influenza vaccine Fluzone® Quadrivalent, administered intramuscularly to children 6 to 35 months of age.

Clinical Study Report for Study 201234 (FLU Q-QIV-022)

This report provides immunogenicity and safety results obtained from Dose 1 (Day 0) up to study conclusion at Day 180.

Development Phase III

IND Number: BB-IND-14466

Name of Investigational Product: GlaxoSmithKline (GSK) Biologicals' Quadrivalent Inactivated Split Virion Influenza Vaccine FLU Q-QIV (GSK2321138A)

Indication Studied: Active immunization against influenza of children 6 to 35 months of age.

Study initiation date:	01-October-2014
Study completion date:	23-June-2015
Data lock point (Date of database freeze):	18-August-2015
Date of report:	Final: 23-September-2015

Sponsor Signatory:	Varsha K. Jain, MD, MPH Director, Clinical Development (Influenza Vaccines), GlaxoSmithKline Biologicals, SA

This study was performed according to the principles of GCP including the archiving of essential documents.

Based on GSK Biologicals' Study Report INS-BIO-CLIN-1010 v05

SYNOPSIS

Name of company: **GlaxoSmithKline Biologicals, SA, Rixensart, Belgium**	**Name of finished product:** GlaxoSmithKline (GSK) Biologicals' Quadrivalent Inactivated Split Virion Influenza Vaccine **FLU Q-QIV** (GSK2282512A)	**Name of active substance:** 15µg each of the following strains: A/H1N1= A/California/7/2009; A/H3N2= A/Texas/50/2012; B/Yamagata=B/Massachusetts/2/2012; B/Victoria= B/Brisbane/60/2008

Study No.: 201234 (FLU Q-QIV-022)

Title of the study:
A Phase III, observer-blind, randomized, controlled, multi-center study to evaluate the immunogenicity and safety of GSK Biologicals' quadrivalent influenza vaccine candidate, GSK2282512A (FLU Q-QIV), compared to Sanofi Pasteur's quadrivalent influenza vaccine *Fluzone® Quadrivalent*, administered intramuscularly to children 6 to 35 months of age.

Investigator(s) and study centre(s):
Multiple centers (69) in Mexico and United States of America (USA).
Principal investigators: This study was conducted by 61 Principal Investigators (PIs) in two countries (2 PIs in Mexico and 59 PIs in the USA).

Publication (reference): None at the time of this report.

Study period: **Study initiation date:** 01-October-2014 **Study completion date:** 23-June-2015 **Data lock point (Date of database freeze):** 18-August-2015	**Phase: III**

Indication: Active immunization against influenza for children 6 to 35 months of age

Objectives:

Primary objective

- To demonstrate the immunogenic non-inferiority of FLU Q-QIV versus *Fluzone Quadrivalent* (in terms of geometric mean titers [GMTs] and SCRs) approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for vaccine-primed and vaccine-unprimed subjects, respectively) in the overall population.

Secondary objective

- If the primary objective was met, the following objective was to be tested:
- CBER's SCR and SPR criteria will be checked for the Q-QIV group for each of the four strains, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for vaccine-primed and vaccine-unprimed subjects, respectively) in the overall population.

Additional secondary objectives

- To describe the immunogenicity (in terms of GMTs, SPRs, SCRs, and mean geometric increases [MGIs]) of FLU Q-QIV and *Fluzone Quadrivalent* for each of the four strains, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed)
- To describe the reactogenicity and safety of FLU Q-QIV and *Fluzone Quadrivalent* overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed) in terms of:
  - Solicited local and general adverse events (AEs) during the 7-day post vaccination follow-up period (day of vaccination and six subsequent days).
  - Unsolicited AEs during the 28-day post-vaccination follow-up period (day of vaccination and 27 subsequent days).
  - Serious adverse events (SAEs), medically attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period
- To evaluate the relative risk of fever after administration of FLU Q-QIV compared to *Fluzone Quadrivalent* during the 2-day post-vaccination follow-up period (day of vaccination and one subsequent day)

Name of company: **GlaxoSmithKline Biologicals, SA, Rixensart, Belgium**	**Name of finished product:** GlaxoSmithKline (GSK) Biologicals' Quadrivalent Inactivated Split Virion Influenza Vaccine **FLU Q-QIV** (GSK2282512A)	**Name of active substance:** 15µg each of the following strains: A/H1N1= A/California/7/2009; A/H3N2= A/Texas/50/2012; B/Yamagata=B/Massachusetts/2/2012; B/Victoria= B/Brisbane/60/2008

Methodology: The study was conducted as a Phase III, observer-blind, randomized, controlled, multi-country, multi-center, self-contained clinical trial with parallel treatment groups.
A total of 2,424 subjects, 6 to 35 months of age, were enrolled and randomized 1:1 to receive either FLU Q-QIV or *Fluzone Quadrivalent*.
Two blood samples were to be collected on Days 0 and 28 for vaccine-primed subjects, and on Days 0 and 56 for vaccine-unprimed subjects.

Study vaccine, dose, mode of administration, lot no.:
Vaccination schedule /site: GSK Biologicals' Quadrivalent Inactivated Split Virion Influenza Vaccine FLU Q-QIV and Sanofi's *Fluzone Quadrivalent* vaccine were to be administered intramuscularly in the deltoid region of the non-dominant arm (subjects ≥ 12 months of age) or anterolateral thigh region (subjects <12 months of age). Vaccine-primed subjects were to receive only 1 dose (Day 0) and vaccine-unprimed subjects were to receive 2 doses (Day 0 and Day 28).

Vaccine composition /dose /lot number: The FLU Q-QIV vaccine contained 15µg Haemaglutinin (HA) each of the A/H1N1, A/H3N2, B/Yamagata and B/Victoria strains (total injected volume was 0.50 mL/dose), while *Fluzone Quadrivalent* contained 7.5 µg of each of the same strains (total injected volume was 0.25 mL/dose).
The lot number for the FLU Q-QIV vaccine was AFLHVA821A and the lot number for the *Fluzone Quadrivalent* vaccine was DLOCA143A.

Study Population: Male or female subjects between and including 6 months and 35 months of age, at the time of the first vaccination, eligible regardless of history of administration of influenza vaccine in a previous season, for whom the investigator believed that their parents/legally acceptable representatives (LARs) would comply with the requirements of the protocol. Written informed consent was obtained from parents/LARs of each subject.

Duration of treatment: The duration of treatment was approximately 28 days or 56 days for each subject depending on their vaccine-priming status.

Criteria for evaluations:

Primary endpoints:

- Humoral immune response to each strain. Serum HI antibody titers for the four strains 28 days after the last vaccine dose was used to calculate
  - GMT ratio (*Fluzone Quadrivalent*/FLU Q-QIV).
  - SCR difference (*Fluzone Quadrivalent* minus FLU Q-QIV).

Secondary endpoints:

- Humoral immune response to each strain, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed). Serum HI antibody on Day 0 and/or 28 days after the last vaccine dose from both groups will be used to calculate:
  - GMTs on Day 0 and 28 days after the last vaccine dose.
  - SPRs on Day 0 and 28 days after the last vaccine dose
  - SCRs 28 days after the last vaccine dose
  - MGIs 28 days after the last vaccine dose
- Solicited local and general AEs, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed):
  - Occurrence of solicited local and general AEs (summarized by incidence rate, intensity, duration and relationship to vaccination [general AEs]) during a 7-day follow-up period (i.e. day of vaccination and six subsequent days) after each vaccination, in each group.

Name of company: **GlaxoSmithKline Biologicals, SA, Rixensart, Belgium**	**Name of finished product:** GlaxoSmithKline (GSK) Biologicals' Quadrivalent Inactivated Split Virion Influenza Vaccine **FLU Q-QIV** (GSK2282512A)	**Name of active substance:** 15µg each of the following strains: A/H1N1= A/California/7/2009; A/H3N2= A/Texas/50/2012; B/Yamagata=B/Massachusetts/2/2012; B/Victoria= B/Brisbane/60/2008

- Unsolicited AEs, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed)
  - Occurrence of unsolicited AEs (summarized by incidence rate, intensity, and relationship to vaccination) during a 28-day follow-up period (i.e. day of vaccination and 27 subsequent days), in each group.
- SAEs, MAEs, and pIMDs, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed
  - Occurrence of SAEs, MAEs and pIMDs (summarized by incidence rate and relationship) during the entire study period
- Occurrence of any fever (≥ 38°C) or Grade 3 fever or higher (> 39°C) during a 2-day follow-up period (i.e. day of vaccination and one subsequent day) after each vaccination

Statistical methods:
The study cohorts analyzed were as follows:

Total vaccinated cohort
The Total vaccinated cohort (TVC) included all vaccinated subjects for whom data were available. Thus, for the analysis of safety, this included all subjects for whom safety data were available and for the analysis of immunogenicity, this included vaccinated subjects for whom immunogenicity endpoint measures were available. The Total vaccinated cohort analysis was performed per treatment actually administered.

According-to-protocol cohort for analysis of safety
The ATP cohort for analysis of safety included all vaccinated and eligible subjects:
- who had received at least 1 dose of study vaccine/comparator according to their random assignment.
- with sufficient data to perform an analysis of safety (1 dose with safety follow-up).
- for whom administration site of the study vaccine was known.
- who had not received a vaccine not specified or forbidden in this protocol.
- who did not meet any of the criteria for elimination from an ATP analysis.

According-to-protocol cohort for analysis of immunogenicity
The ATP cohort for analysis of immunogenicity in terms of antibody response measured by the HI assay included all evaluable subjects (i.e., who meet all eligibility criteria, who complied with the procedures and intervals specified in the protocol, with no elimination criteria assigned during the study) for whom data concerning immunogenicity endpoint measures were available. This included subjects for whom assay results were available for antibodies against at least 1 study vaccine antigen component after vaccination and:
- whose samples were collected within the interval allowed as defined in the protocol
- who did not meet any of the criteria for elimination from an ATP analysis
- who did not present a medical condition leading to exclusion from an ATP analysis

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Analysis of demographics and other baseline characteristics

- Demographic characteristics (age at first study vaccination , height and weight, gender, and race), were summarized by study group, age strata (all ages, 6-17, and 18-35 months of age) and priming status (primed and unprimed) using descriptive statistics:
  - Frequency tables were generated for categorical variable such as center
  - Mean, median and standard deviation were provided for continuous data such as age.
  - Summary statistics for subjects' age classified by gender of the vaccinated subjects, as a whole, and per study group, were calculated
  - The distribution of subjects enrolled among the study sites was tabulated as a whole and per group and classified subjects into disposition categories, including subjects who entered, completed, or withdrew from the study
  - The proportion of subjects with prior immunologic experience with influenza vaccine(s) in the previous 3 influenza seasons were tabulated for each study group.

Analysis of immunogenicity

The primary analysis was based on the ATP cohort for analysis of immunogenicity. Since the percentage of vaccinated subjects excluded from the ATP cohort for analysis of immunogenicity was more than 5%, a second analysis based on the Total vaccinated cohort was performed to complement the ATP analysis.

Within groups assessment

- For the humoral immune response in terms of anti-HA antibodies against each of the 4 vaccine influenza strains, the following parameters (with 95% CIs) were calculated by each treatment group (FLU Q-QIV and Fluzone Quadrivalent) for all subjects, by age stratum (6 to 17 and 18 to 35 months of age) and by priming status (vaccine-primed and -unprimed):
  - GMTs of anti-HA antibody titers at Day 0 and Day 28 following last vaccination
  - SCRs at Day 28 following last vaccination.
  - SPRs at Day 0 and Day 28 following last vaccination.
  - MGI at Day 28 following last vaccination.

Between groups assessment

- The GMT ratio and difference in SCR between groups were calculated to assess the immunogenic non-inferiority of FLU Q-QIV compared to Fluzone Quadrivalent:
- The GMT ratio of *Fluzone Quadrivalent* over FLU Q-QIV and the two-sided 95% CI for each of the strains was calculated.
- The difference of SCR (*Fluzone Quadrivalent* minus FLU Q-QIV) and the two-sided 95% CI for each of the strains was calculated.

The non-inferiority of FLU Q-QIV to Fluzone Quadrivalent was to be concluded if the upper limit of the two-sided 95% CI for the GMT ratio (Fluzone Quadrivalent/FLU Q-QIV) was ≤ 1.5 and the upper limit of the two-sided 95% CI on the SCR difference (Fluzone Quadrivalent minus FLU Q-QIV) was ≤ 10% for all strains in the overall population.

Analysis of safety

The primary analysis was performed on the Total vaccinated cohort.

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Within groups assessment

- For the analysis of vaccine safety, the following parameters (with 95% CI) were calculated by each treatment group for all subjects, by age stratum (6 to 17 and 18 to 35 months of age) and by priming status (primed, unprimed):
  - The percentage of subjects with at least one solicited local AE, with at least one solicited general AE and with any AE during the 7-day follow-up period were tabulated with exact 95% CI after each vaccine dose and overall. The percentage of doses followed by at least one solicited local AE, with at least one solicited general AE, and with any AE during the defined follow-up period, was tabulated with exact 95% CI. The same calculations were performed for symptoms rated as Grade 3, related AEs and Grade 3 related AEs.
  - The percentage of subjects reporting each individual solicited local (any, Grade 3, and medically attended) and general (any, Grade 3, related, Grade 3 related, and medically attended) AE during the 7-day solicited follow-up period were tabulated with exact 95% CI. All solicited local AEs were considered to be causally related. The percentage of doses followed by each individual solicited local and general AE during the 7-day solicited follow-up period were tabulated with exact 95% CI. The duration of the solicited symptoms were also be tabulated.
  - The verbatim reports of unsolicited AEs that were reviewed by a physician and the signs and symptoms were coded according to the MedDRA. The percentage of subjects with at least one report of AE classified by MedDRA and reported up to 27 days after vaccination were tabulated with exact 95% CI. The same tabulation was performed for Grade 3 unsolicited AEs, for unsolicited AEs with a relationship to vaccination and Grade 3 unsolicited AEs with relationship to vaccination.
  - MAEs, SAEs, and pIMDs were collected and summarized through the entire study period (180 days). In addition, SAEs and withdrawal due to AEs were described in detail.

Between groups assessment (exploratory analysis)

As an exploratory analysis, the relative risk of subjects with any fever (≥ 38°C) and Grade 3 or higher fever (> 39°C) during two days (48 hours) follow-up after any vaccine dose from the two vaccine groups was calculated for all subjects along with the 95% CI. However, these results (relative risks) should be interpreted with caution since no multiplicity adjustments were made.

Synopsis Table 1: Study population (Total Vaccinated cohort):

Number of subjects	**Q-QIV**	**F-QIV**	**Total**
Planned, N	1200	1200	2400
Randomised, N (Total Vaccinated Cohort)	1207	1217	2424
Completed, n (%)	1132 (93.8)	1139 (93.6)	2271 (93.7)
Demographics	Q-QIV	F-QIV	Total
N (Total Vaccinated Cohort)	1207	1217	2424
Females:Males	547:660	582:635	1129:1295
Mean Age, months (SD)	19.4 (8.7)	19.5 (8.9)	19.5 (8.8)
Median Age, months (minimum, maximum)*	19 (6, 35)	19 (6, 36*)	19 (6, 36*)
White - Caucasian / European Heritage, n (%)	770 (63.8)	781 (64.2)	1551 (64.0)
African Heritage / African American, n (%)	190 (15.7)	187 (15.4)	377 (15.6)
Other, n (%)	183 (15.2)	172 (14.1)	355 (14.6)

Q-QIV = Flu Q-QIV; F-QIV = Fluzone Quadrivalent

N = total number of subjects; n/% = number/percentage of subjects; SD = standard deviation

*Pid (b) (6) in the F-QIV group was 36 months of age and was included in the 18-35 months of age subgroup

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Summary:

Immunogenicity results:

- The confirmatory primary objective to demonstrate immunogenic non-inferiority of FLU Q-QIV compared to *Fluzone Quadrivalent* vaccine in children 6-35 months of age 28 days after the last vaccination, was met for all four vaccine strains since the immunogenic response elicited by FLU Q-QIV fulfilled CBER's immunogenicity criteria (in terms of adjusted GMT ratio and difference in SCRs) for non-inferiority to a comparator vaccine.
  - The CBER criteria specify an UL of the 2-sided 95% CI for the adjusted GMT ratio of ≤1.5 (the range of adjusted GMT ratios for F-QIV/Q-QIV was 0.69 to 0.95 for the 4 strains), and an UL of the 2-sided 95% CI for the difference in SCRs of ≤10% (the range of difference in SCRs for F-QIV minus Q-QIV was -12.02% to -2.27% for the 4 strains).

Synopsis Table 2: Adjusted GMT ratios for the immunogenic response at 28 days after the last vaccine dose: F-QIV/Q-QIV (ATP cohort for immunogenicity)

					Adjusted GMT ratio (F-QIV / Q-QIV)		
	F-QIV		Q-QIV			95% CI	
Antibody	**N**	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1)	980	85.1	972	99.6	0.85	0.77	0.95
A/Texas/50/2012 (H3N2)	980	84.6	972	99.8	0.85	0.77	0.94
B/Massachusetts/2/2012 (Yamagata)	980	167.3	974	258.1	0.65	0.59	0.71
B/Brisbane/60/2008 (Victoria)	980	33.7	973	54.5	0.62	0.56	0.69

Q-QIV = Flu Q-QIV; F-QIV = Fluzone Quadrivalent
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Synopsis Table 3: SCR Difference between treatment groups at 28 days after the last vaccine dose: F-QIV minus Q-QIV (ATP cohort for immunogenicity)

							Difference in SCR (F-QIV minus Q-QIV)		
	F-QIV			Q-QIV				95% CI	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
A/California/7/2009 (H1N1)	980	660	67.3	972	716	73.7	-6.32	-10.34	-2.27
A/Texas/50/2012 (H3N2)	980	680	69.4	972	740	76.1	-6.74	-10.68	-2.80
B/Brisbane/60/2008 (Victoria)	980	475	48.5	973	631	64.9	-16.38	-20.68	-12.02
B/Massachusetts/2/2012 (Yamagata)	980	723	73.8	974	833	85.5	-11.75	-15.28	-8.21

Q-QIV = Flu Q-QIV; F-QIV = Fluzone Quadrivalent
SCR defined as:
- For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
- For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

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- A secondary immunogenicity objective was to assess whether the HI response elicited by FLU Q-QIV in children 6-35 months of age 28 days after the last vaccination, met CBER's SCR and SPR criteria for acceptable immunogenicity. The study results indicated that, with the exception of the SPR for the B/Victoria strain, the FLU Q-QIV immunogenic response met the SCR and SPR criteria.
  - The CBER criteria specify a LL of the 2-sided 95% CI for the SCR of ≥ 40% (the range for Q-QIV was 61.8% to 83.2% for the 4 strains), and a LL of the 2-sided 95% CI for the SPR of ≥ 70% (the value for the B/Victoria strain was 63.0% and the range for the other 3 strains was 77.8% to 95.8%)

Synopsis Table 4: Seroconversion rates (SCRs) 28 days after the last vaccine dose for FLU Q-QIV and FLU F-QIV (ATP cohort for immunogenicity)

			SCR			
					95% CI	
Antibody	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/California/7/2009 (H1N1)	Q-QIV	972	716	73.7	70.8	76.4
	F-QIV	980	660	67.3	64.3	70.3
A/Texas/50/2012 (H3N2)	Q-QIV	972	740	76.1	73.3	78.8
	F-QIV	980	680	69.4	66.4	72.3
B/Massachusetts/2/2012 (Yamagata)	Q-QIV	974	833	85.5	83.2	87.7
	F-QIV	980	723	73.8	70.9	76.5
B/Brisbane/60/2008 (Victoria)	Q-QIV	973	631	64.9	61.8	67.9
	F-QIV	980	475	48.5	45.3	51.6

Q-QIV = Flu Q-QIV; F-QIV = Fluzone Quadrivalent
SCR defined as :
- For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
- For initially seropositive subjects antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

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Synopsis Table 5: Seropositivity rates, seroprotection rates (SPR), and GMTs at Day 0 and 28 days after the last vaccine dose (ATP cohort for immunogenicity)

				Seropositivity rate (≥ 10 1/DIL)				SPR (≥ 40 1/DIL)				GMT		
						95% CI				95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
California/7/2009 H1N1	Q-QIV	PRE	972	347	35.7	32.7	38.8	191	19.7	17.2	22.3	11.0	10.2	12.0
		POST	1013	947	93.5	91.8	94.9	814	80.4	77.8	82.8	98.8	90.3	108.2
	F-QIV	PRE	980	363	37.0	34.0	40.2	190	19.4	17.0	22.0	11.1	10.2	12.0
		POST	1028	935	91.0	89.0	92.6	775	75.4	72.6	78.0	84.4	76.9	92.6
A/Texas/50/2012 H3N2	Q-QIV	PRE	972	322	33.1	30.2	36.2	135	13.9	11.8	16.2	9.2	8.6	9.8
		POST	1013	982	96.9	95.7	97.9	833	82.2	79.7	84.5	97.7	90.3	105.7
	F-QIV	PRE	980	315	32.1	29.2	35.2	140	14.3	12.2	16.6	9.6	8.9	10.3
		POST	1028	978	95.1	93.6	96.4	800	77.8	75.2	80.3	84.3	77.6	91.6
B/Massachusetts/2/2012 Yamagata	Q-QIV	PRE	974	689	70.7	67.8	73.6	324	33.3	30.3	36.3	20.3	18.8	22.0
		POST	1013	1013	100	99.6	100	983	97.0	95.8	98.0	257.5	240.9	275.3
	F-QIV	PRE	980	683	69.7	66.7	72.6	336	34.3	31.3	37.4	20.6	19.0	22.4
		POST	1028	1020	99.2	98.5	99.7	911	88.6	86.5	90.5	164.2	151.8	177.6
B/Brisbane/60/2008 Victoria	Q-QIV	PRE	973	130	13.4	11.3	15.7	40	4.1	3.0	5.6	6.2	6.0	6.5
		POST	1013	939	92.7	90.9	94.2	669	66.0	63.0	69.0	55.1	50.8	59.8
	F-QIV	PRE	980	124	12.7	10.6	14.9	46	4.7	3.5	6.2	6.3	6.0	6.6
		POST	1028	837	81.4	78.9	83.8	512	49.8	46.7	52.9	33.4	30.6	36.4

Q-QIV = Flu Q-QIV;F-QIV = Fluzone Quadrivalent
Seroprotection = HI antibody titre ≥ 40 1/DIL
GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Visit Day 0; POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Safety results:

- *Overall incidence of solicited adverse events (AEs):* During the 7-day post-vaccination period, at least one solicited AE was reported for 74.1% and 71.6% of subjects in the Q-QIV and F-QIV groups, respectively. At least one grade 3 solicited AE was reported for 11.0% and 8.1% of subjects in the Q-QIV and F-QIV groups, respectively. At least one solicited AE related to vaccination was reported for 68.2% and 65.7% of subjects in the Q-QIV and F-QIV groups, respectively. At least one grade 3 solicited AE related to vaccination was reported for 9.4% and 6.9% of subjects in the Q-QIV and F-QIV groups, respectively.
- *Solicited local AEs:* Overall, during the 7-day post-vaccination period, injection site pain was the most frequently reported solicited local AE (44.0% and 40.1% of subjects in the Q-QIV and F-QIV groups, respectively). Grade 3 injection site pain was reported for 2.9% and 1.7% of subjects, respectively.
- *Solicited general AEs:* Overall, during the 7-day post-vaccination period, irritability/ fussiness was the most frequently reported solicited general AE (54.4% and 50.5% of subjects in the Q-QIV and F-QIV groups, respectively) followed by drowsiness (40.6% and 40.9% of subjects, in the Q-QIV and F-QIV groups, respectively) and loss of appetite (33.7% and 33.4% of subjects in the Q-QIV and F-QIV groups, respectively).

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- *Relative risk of fever:* The relative risk of any fever (≥38°C) for the subjects in the Q-QIV group compared to the subjects in the F-QIV group, during a 2-day (48 hours) follow-up period was 0.97 (overall/subject, 3.6% for Q-QIV vs. 3.7% for F-QIV) with a 95% CI of [0.62; 1.52] (p-value = 0.9777). The relative risk of grade 3 or above fever (>39.0°C) for subjects in the Q-QIV group compared to the subjects in the F-QIV group, during a 2-day (48 hours) follow-up period was 1.49 (overall/subject, 0.8% for Q-QIV vs. 0.5% for F-QIV) with a 95% CI of [0.47; 5.09] (p-value = 0.6156).
- *Unsolicited AEs*: During the 28-day post-vaccination period, at least one unsolicited AE was reported for 45.5% and 44.1% of subjects in the Q-QIV and F-QIV groups, respectively. Upper respiratory tract infection was the most frequently reported AE in both the Q-QIV and F-QIV groups (in 9.2% and 8.4% of subjects, respectively). At least one grade 3 unsolicited AE was reported for 5.8% and 6.2% subjects in the Q-QIV and F-QIV groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 5.9% and 5.8 % of subjects, respectively. At least one grade 3 unsolicited AE with causal relationship to vaccination was reported for 0.6% and 0.7% subjects, respectively.
- *MAEs*: At least one unsolicited AE with a medically attended visit during the entire study period was reported for 60.2% and 59.1% of subjects in the Q-QIV and F-QIV groups, respectively. Upper respiratory tract infection was the most frequently reported MAE in both groups (20.1% and 19.1% of subjects in the Q-QIV and F-QIV groups, respectively) followed by otitis media (16.1% and 18.2% of subjects in the Q-QIV and F-QIV groups, respectively).
- *pIMDs*: There were two cases of pIMDs reported during the entire study period and both occurred after the first vaccination dose, but neither was assessed by the investigator as causally related to vaccination. One pIMD was in the Q-QIV group (Kawasaki's disease, also reported as an SAE; recovering/resolving at the time of this report) and the other in the F-QIV group (Erythema multiforme; reported recovered/resolved at the time of this report).
- *SAEs*: A total of 56 non-fatal SAEs were reported for 43 subjects during the entire study period. Of these, 29 SAEs were experienced by 22 subjects (1.8%) in the Q-QIV group and 28 SAEs were reported for 21 subjects (1.7%) in the F-QIV (*Fluzone Quadrivalent*) group. No SAE was deemed by the investigator to be causally related to vaccination. All SAEs in the Q-QIV group were reported as resolved/recovered with the exception of one case of Kawasaki's disease and one case of croup, which were reported as resolving/recovering at the time of this report. All SAEs in the F-QIV group were also reported as resolved/recovered at the time of this report, with the exception of 4 SAEs (B precursor type acute leukaemia, failure to thrive, developmental delay and hemiplegia) reported in 3 subjects. No fatal events were reported during the entire study period.
- *Risk factors in the RMP:* Risk factors being considered for inclusion in the Q-QIV Risk Management Plan were to be reported as SAEs per study protocol. There were 9 cases of such a risk, febrile seizure (4 subjects in the F-QIV group and 5 subjects in the Q-QIV group). All 9 events were reported as resolved/recovered and none were assessed by the investigator as causally related to vaccination.

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Conclusion:

- In children 6-35 months of age, Q-QIV was immunogenically non-inferior to F-QIV in terms of GMT ratio and SCR difference for all four strains contained in the vaccine.
- Q-QIV met CBER's SCR and SPR criteria in children 6-35 months of age 28 days after the last vaccination with the exception of the SPR criterion for the B/Brisbane/60/2008 (Victoria) strain.
- A full dose of Q-QIV (0.5mL) was more immunogenic with respect to the influenza B strains (post-hoc analysis) without incremental reactogenicity or safety effects in all subjects 6-17 months of age and in vaccine-unprimed subjects 6-35 months of age, as compared to the 0.25mL dose used for the F-QIV comparator.
- Q-QIV and F-QIV had similar reactogenicity and safety profiles.
- Q-QIV and F-QIV were generally well tolerated with no safety concerns.

Date of report: Final: 23-September-2015

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LIST OF ABBREVIATIONS

AE:	Adverse event
ATP:	According-To-Protocol
CBER:	Center for Biologics Evaluation and Research
CDC:	Centers for Disease Control
CHMP:	Committee for Medicinal Products for Human Use
CI:	Confidence Interval
CSR:	Clinical Study Report
eCRF:	electronic Case Report Form
ELISA:	Enzyme-Linked Immunosorbent Assay
EMA:	European Medicines Agency
(e)TDF	(electronic) temperature excursion decision form
FDA:	Food and Drug Administration (United States)
GCP:	Good Clinical Practice
GMT:	Geometric Mean Titer
GSK:	GlaxoSmithKline
GVCL:	Global Vaccines Clinical Laboratories
HA:	Haemagglutinin
H(A)I:	Haemagglutination Inhibition
IB	Investigator Brochure
ICF:	Informed Consent Form
ICH:	International Conference on Harmonization
IEC:	Independent Ethics Committee
IM:	Intramuscular(ly)
IND:	Investigational New Drug

IRB:	Institutional Review Board
LAR:	Legally Acceptable Representative
MAE:	Medically Attended Adverse Event
MedDRA:	Medical Dictionary for Regulatory Activities
MGI:	Mean Geometric Increase
OOS	Out of Specificatio
pIMD:	Potential Immune-Mediated Disease
Q:	Quebec
QIV:	Quadrivalent Influenza Vaccine
RDE:	Remote Data Entry
RMP:	Risk Management Plan
SAE:	Serious Adverse Event
SBIR:	Randomization System on Internet
SCR:	Seroconversion Rate
SDV:	Source Document Verification
SPM:	Study Procedures Manual
SPR:	Seroprotection Rate
TIV:	Trivalent Influenza Vaccine
TVC:	Total vaccinated cohort
US:	United States
WHO:	World Health Organization

GLOSSARY OF TERMS

Adverse event (AE):	Any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.
Blinding:	A procedure in which one or more parties to the trial are kept unaware of the treatment assignment in order to reduce the risk of biased study outcomes. The level of blinding is maintained throughout the conduct of the trial, and only when the data are cleaned to an acceptable level of quality will appropriate personnel be unblinded or when required in case of a serious adverse event (SAE). In an observer-blind study, the subject and the site and sponsor personnel involved in the clinical evaluation of the subjects are blinded while other study personnel may be aware of the treatment assignment.
Child in care:	A child who has been placed under the control or protection of an agency, organisation, institution or entity by the courts, the government or a government body, acting in accordance with powers conferred on them by law or regulation. The definition of a child in care can include a child cared for by foster parents or living in a care home or institution, provided that the arrangement falls within the definition above. The definition of a child in care does not include a child who is adopted or has an appointed legal guardian.
Eligible:	Qualified for enrolment into the study based upon strict adherence to inclusion/exclusion criteria.

Epoch:	An epoch is a self-contained set of consecutive time points or a single time point from a single protocol. Self-contained means that data collected for all subjects at all time points within that epoch allows to draw a complete conclusion to define or precise the targeted label of the product (e.g. primary, booster, yearly immunogenicity follow-ups, and surveillance periods for efficacy or safety.
eTrack:	GlaxoSmithKline's tracking tool for clinical trials.
Evaluable:	Meeting all eligibility criteria, complying with the procedures defined in the protocol, and, therefore, included in the according-to-protocol (ATP) analysis.
Geometric Mean Titer (GMT):	The anti-log of the mean of the log (base 10) transformed inverse titers (the number X would denote the inverse of a titer expressed as "1:X"). Antibody titers below the cut off of the assay are given an arbitrary value of half the cut-off for the purpose of GMT calculation.
Immunological correlate of protection:	The defined humoral antibody response above which there is a high likelihood of protection in the absence of any host factors that might increase susceptibility to the infectious agent.
Investigational vaccine/product: **(Synonym of Investigational Medicinal Product)**	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
Mean Geometric Increase (MGI):	MGI is defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal haemagglutination inhibition (HI) titer to the pre-vaccination (Day 0) reciprocal HI titer.
Potential Immune-Mediated Disease (pIMD):	Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology.

Primary completion date:	The date that the final subject was examined or received an intervention for the purpose of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated.
Randomisation:	Process of random attribution of treatment to subjects in order to reduce bias of selection.
Risk Management Plan (RMP):	According to the guidance from the European Medicines Agency (EMA), the RMP is a plan to manage a known or potential risk associated with a medicine. Its purpose is to allow patient's continued access to certain medicines for which there are safety concerns that may be managed through appropriate use. The RMP includes information on a medicine's safety profile; how its risks will be prevented or minimised in patients; plans for studies and other activities to gain more knowledge about the safety and efficacy of the medicine; risk factors for developing side effects; and measuring the effectiveness of risk minimisation measures.
Self-contained study:	Study with objectives not linked to the data of another study.
Serious Adverse Event (SAE):	Any untoward medical occurrence in a patient or clinical investigation subject that: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.
Seroconversion Rate (SCR):	SCR is defined as the proportion of vaccinees who have either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least a four-fold increase in post-vaccination titer.
Seroprotection Rate (SPR):	The seroprotection rate or SPR is defined as the proportion of vaccinees with a serum HI titer ≥ 1:40.
Site monitor:	An individual assigned by the sponsor who is responsible for assuring proper conduct of clinical studies at one or more investigational sites.
Solicited AE:	AEs to be recorded as endpoints in the clinical study. The presence/occurrence/intensity of these events is actively solicited from the subject or an observer during a specified post-vaccination follow-up period.

Sub-cohort:	A group of subjects for whom specific study procedures are planned as compared to other subjects.
Subject:	Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the clinical study, either as a recipient of the vaccine(s)/product(s) or as a control.
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the study.
Treatment:	Term used throughout the clinical study to denote a set of investigational product(s) or marketed product(s) or placebo intended to be administered to a subject, identified by a unique number, according to the study randomisation or treatment allocation.
Treatment number:	A number identifying a treatment to a subject, according to the study randomisation or treatment allocation.
Unsolicited AE:	Any AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited AE.
Vaccine-primed subjects:	All subjects (6 to 35 months of age) who have received a total of two or more doses of seasonal influenza vaccine since 01 July 2010 or at least 1 dose of the 2013-2014 seasonal influenza vaccine. These subjects will receive only one dose of seasonal influenza vaccine in this study.
Vaccine-unprimed subjects:	All subjects (6 to 35 months of age) who have never received any seasonal influenza vaccine or have received only one dose of seasonal influenza vaccine since 01 July 2010, but did NOT receive any 2013-2014 seasonal influenza vaccine. These subjects will receive two doses (28 days apart) of seasonal influenza vaccine in this study.

TRADEMARKS

The following trademarks are used in the present report.

Note: In the body of the Study Report, the names of the vaccines/products and/or medications will be written without the superscript symbol ™ or ® and in *italics*.

Trademarks of the GlaxoSmithKline group of companies	Generic description
FluLaval™ Quadrivalent	Quadrivalent influenza vaccine (inactivated, split virion)

Trademarks not owned by the GlaxoSmithKline group of companies	Generic description
Fluzone® Quadrivalent (Sanofi Pasteur)	Inactivated Quadrivalent Split Virion Influenza Vaccine
Fluzone® (Sanofi Pasteur)	Inactivated Trivalent Split Virion Influenza Vaccine

1. ETHICS

1.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, any amendments, the informed consent, and other information that required pre-approval were reviewed and approved by the IECs and IRBs of each study centre in Mexico and the United States of America (USA).

1.2. Ethical conduct of the study

Overall this study was to be conducted in accordance with ethical principles that have their origins in the Declaration of Helsinki, the principles of "good clinical practice" (GCP) and all applicable regulatory requirements.

During the course of the study, whenever potential issues with regard to the conduct of the study were identified, either via site monitoring activities or brought to GlaxoSmithKline (GSK) Biologicals' attention by other oversight mechanisms, these issues were investigated and appropriate corrective and / preventive actions where possible were taken.

Refer to Section 5.11 for further details regarding the GCP issues and corrective actions.

1.3. Subject information and consent

Written informed consent was to be obtained from each subject's parent(s)/LAR(s) prior to the performance of any study-specific procedures.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

This multicenter study, sponsored by GSK Biologicals, was conducted by 61 principal investigators across 69 centers in Mexico and USA. Dr. Rodriguez-Weber from Mexico, Dr. Joseph Domachowske, and Dr. Michael Leonardi, both from the USA, were identified as the principal investigators to review and approve this report.

Contract Research Organizations (CROs) were employed to perform the following functions according to an agreed contract. The CRO responsibilities were conducted according to GSK's SOPs or SOPs agreed between GSK and the CRO. The following contract organizations were involved in this study:

Clinical Study Monitoring and Site Management: Novella Inc. was used as a monitoring service in the USA. Monitoring was not outsourced in Mexico.

Sample management:

Quest Diagnostics (central laboratory) was contracted for interim sample storage (but no analysis).

Quest Diagnostics
26081 Avenue Hall, ≠ 150
Valencia, CA 91355, USA

Data Management activities:

Tata Consultancy Services
Millennium Business Park, Waterfall Plaza,
Building No.4/303, Sector 2, Mahape,
Navi Mumbai, 400 710
India

3. INTRODUCTION

Influenza is a serious public health problem; it has a high incidence in the human population and causes regular large-scale morbidity and mortality. During seasonal epidemics, 5-15% of the worldwide population is typically infected, resulting in 3-5 million cases of severe illness and a quarter to half a million excess deaths annually. Most deaths associated with influenza in industrialised countries occur among people aged 65 years or older [World Health Organisation (WHO), 2009], although infection is most common in children [O'Brien, 2004; Izurieta, 2000]. In particular, children younger than 5 years of age have incidence rates of severe influenza disease and hospitalisation due to influenza second only to the elderly population.

The highest influenza burden in terms of paediatric respiratory admissions is seen in infants 6 to 11 months of age [Schanzer, 2006] and rates of illness in children younger than 2 years of age are substantially higher than those in children 2 years of age or older [Centers for Disease Control (CDC), 2007; Poehling, 2006]. Children also play an important role in the spread of the disease [Brownstein, 2008], possibly because of their high levels of virus shedding. Since annual influenza vaccination is currently the most effective means of controlling influenza and preventing its complications and mortality [WHO, 2009], there is a general trend to extend the recommendation for influenza vaccinations not only to infants with high risk of complications, but also to healthy children and adolescents. The effectiveness of influenza vaccination is, however, dependent on adequate matching between the circulating viruses and the viruses contained in the vaccine.

Since 1983, two antigenically distinct lineages of influenza B have circulated in the world. Their co-existence has also resulted in the emergence and subsequent worldwide circulation of a reassortant B virus possessing a Victoria-lineage haemagglutinin (HA) with a Yamagata-lineage derived neuraminidase [Barr, 2006]. In the United States (US), both Yamagata and Victoria lineages have co-circulated since the 2001-2002 influenza season.

Sera from adults vaccinated with the virus from one B lineage show some modest level of cross-reactivity against the other B lineage *in vitro*, which may be due to a prior natural exposure or vaccine priming [Barr, 2006; Heckler, 2007]. However, infants and children are much less likely to generate such a cross-reactive antibody response, presumably because of limited prior immunologic experience with influenza, and thus may be more susceptible than adults to infection with a co-circulating alternate lineage B strain. In a study of unimmunised (vaccine-unprimed) infants, no measurable cross-reactive antibodies to the alternate B lineage were found in the sera of naïve children after their first vaccine exposures [Hannoun, 2004; Heckler, 2007; Hobson, 1972].

From 2001 to 2009, influenza B viruses have accounted for 6.9% to 38.7% of clinical isolates from CDC surveillance [CDC, 2010]. In five of these eight years, a substantial proportion of B virus isolates have been representative of the genetic lineage not included in the trivalent influenza vaccine (TIV), and have accounted for 6.4% to 29.9% (median of 8.5%) of all influenza virus isolates [CDC, 2010].

The consequences of such a B virus mismatch could be severe. During the 2007-2008 season, almost 30% of influenza viruses tested at the CDC in the US were type B, and 98% of them did not match the lineage contained in the TIV influenza vaccine [CDC, 2008]. Assuming that a quadrivalent influenza vaccine (QIV) containing a second B strain had been used in the 2007-2008 season rather than a TIV vaccine, a public health impact model for influenza-associated health outcomes estimated that the QIV seasonal vaccine could have prevented an additional 1,090,514 influenza cases, and resulted in 7,488 fewer hospitalisations and 321 fewer deaths [Reed, 2009]. Since the two evolutionarily distinct lineages of influenza B virus continue to co-circulate, and cross-reactivity between the two lineages is low in the paediatric population (which has limited immunologic experience with influenza), an additional B strain antigen in the seasonal vaccine may offer greater efficacy and broader protection to children [Englund, 2006; Levandowski, 1991]. In addition, the 2007-2008 experience suggested that mismatched B virus morbidity was substantial in the elderly [Proff, 2009]; and these vulnerable persons could benefit from improved herd immunity in children as well as direct immunisation. These considerations have lead GlaxoSmithKline (GSK) Biologicals to develop QIV seasonal vaccines, comprised of two A and two B strains, since 2008.

FluLaval Quadrivalent (hereafter referred to as FLU Q-QIV) is a split virion, inactivated, QIV candidate influenza vaccine consisting of four monovalent viral antigen bulks (prepared from influenza strains A/H1N1, A/H3N2, B/Victoria lineage and B/Yamagata lineage). FLU Q-QIV is manufactured using minor modifications of the process used to prepare the currently licensed *FluLaval*, a TIV influenza vaccine manufactured in Quebec, Canada. *FluLaval* was first approved (under the trade name *Fluviral*) on 18 December 1992 in Canada and is currently available in 16 countries, including the US where it is approved for administration to persons 3 years of age and older. The FLU Q-QIV candidate vaccine is produced by including an additional B strain; one dose of the split inactivated vaccine contains 15 µg HA for each of the four influenza virus strains, for a total of 60 µg HA/0.5 mL dose. To date, six completed clinical studies have evaluated FLU Q-QIV: three studies in paediatric subjects 6 months to 17 years of age (studies FLU Q-QIV-003, FLU Q-QIV-006, FLU Q-QIV-013, FLU Q-QIV-021) and two

studies in adult subjects 18 years of age and above, including elderly subjects > 64 years of age (studies FLU Q-QIV-007 and FLU Q-QIV-[T+]-009). The safety and reactogenicity profile of the FLU Q-QIV candidate vaccine, as evaluated in 1,384 adult subjects (including elderly) and in 4,274 children 6 months to 17 years of age, was generally consistent with that after administration of licensed TIV seasonal vaccines.

Fluzone Quadrivalent is a split virion, inactivated QIV vaccine licensed in the US for use in persons 6 months of age and above. *Fluzone Quadrivalent* is formulated with two influenza A strains and two influenza B strains. The approved 0.25 mL dose for children 6 to 35 months of age contains 7.5 µg HA for each of the four influenza virus strains, for a total of 30 µg HA/0.25 mL dose.

This study is designed to demonstrate non-inferiority of FLU Q-QIV to a US-licensed vaccine in children 6 to 35 months of age, which will serve as the pivotal evidence for licensure. *Fluzone Quadrivalent* was chosen as a comparator since it is currently the only QIV vaccine licensed in the US in children from 6 months old onwards.

4. STUDY OBJECTIVES

4.1. Primary objective

- To demonstrate the immunogenic non-inferiority of FLU Q-QIV versus *Fluzone Quadrivalent* (in terms of geometric mean titers [GMTs] and SCRs) approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for vaccine-primed and vaccine-unprimed subjects, respectively) in the overall population.

  Criteria to conclude non-inferiority of FLU Q-QIV:

  Non-inferiority of FLU Q-QIV was demonstrated if:

  – *the upper limit of the two-sided 95% confidence interval (CI) for the GMT ratio (Fluzone Quadrivalent/FLU Q-QIV) does not exceed 1.5 for each of the four strains, and*

  – *the upper limit of the two-sided 95% CI for the difference in SCR (Fluzone Quadrivalent minus FLU Q-QIV) does not exceed 10% for each of the four strains.*

4.2. Secondary objectives

If the primary objective was met, the following objective would be tested:

- CBER's SCR and SPR criteria were checked for the Q-QIV group for each of the four strains, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for vaccine-primed and vaccine-unprimed subjects, respectively) in the overall population.

CBER criteria:

- *the lower limit of the two-sided 95% CI for SCR should be ≥ 40% for each strain.*
- *the lower limit of the two-sided 95% CI for SPR should be ≥ 70% for each strain.*

Additional secondary objectives:

- To describe the immunogenicity (in terms of GMTs, SPRs, SCRs, and mean geometric increases [MGIs]) of FLU Q-QIV and *Fluzone Quadrivalent* for each of the four strains, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed).
- To describe the reactogenicity and safety of FLU Q-QIV and *Fluzone Quadrivalent* overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed) in terms of:
  - Solicited local and general adverse events (AEs) during the 7-day post vaccination follow-up period (day of vaccination and six subsequent days).
  - Unsolicited AEs during the 28-day post-vaccination follow-up period (day of vaccination and 27 subsequent days).
  - Serious adverse events (SAEs), medically attended adverse events (MAEs) and potential immune-mediated diseases (pIMDs) during the entire study period.
- To evaluate the relative risk of fever after administration of FLU Q-QIV compared to *Fluzone Quadrivalent* during the 2-day post-vaccination follow-up period (day of vaccination and one subsequent day).

4.3. Exploratory objective

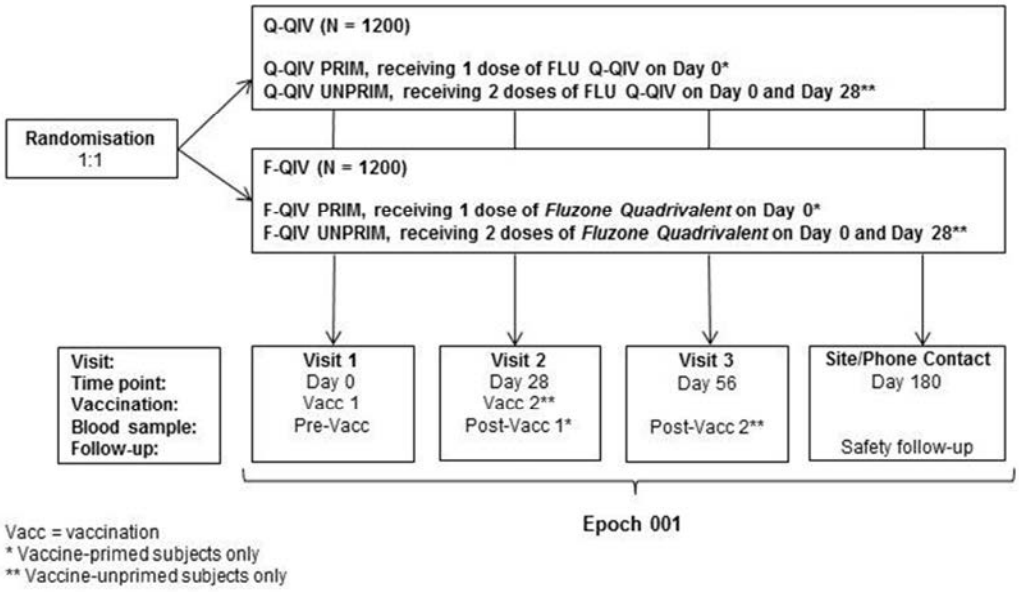
- Exploratory testing using Enzyme-Linked Immunosorbent Assay (ELISA), other immunoassay formats, or functional assays such as a virus neutralization test or a neuraminidase-inhibition test to assess the anti-influenza virus antibody responses elicited by vaccination may be performed depending on samples and testing availability.

5. INVESTIGATIONAL PLAN

5.1. Study design

5.1.1. Overall study design – Description

The diagram below presents the overall design of the study.



The study was conducted as a Phase III, observer-blind, randomized, controlled, multi-country, multi-center, self-contained clinical trial with parallel treatment groups.

Duration of the study: Approximately 6 months for each enrolled subject to complete the study.

- **Treatment allocation:** Subjects 6-35 months of age randomized 1:1 to receive either FLU Q-QIV or *Fluzone Quadrivalent*.
    - Age (6-17 and 18-35 months), study center, and the pre-study influenza vaccine priming status of the subjects were minimization factors to ensure balanced representation of the combination of the minimization factors in the two study groups. The study aimed to enroll at least 40% but no more than 50% of the total subjects in the age group of 6-17 months of age.
- **Vaccination schedules:**
    - Vaccine-primed* subjects: one intramuscular (IM) injection, on Day 0.
    - Vaccine-unprimed* subjects: two IM injections, on Days 0 and 28.

    * See GLOSSARY OF TERMS for the definitions of vaccine-primed and -unprimed subjects.

- **Sampling schedule:** Blood samples were collected on Days 0 and 28 for vaccine-primed subjects and on Days 0 and 56 for vaccine-unprimed subjects.

5.1.2. Discussion of study design

According to the FDA Guidance for Industry on Clinical Data Needed to Support the Licensure of Seasonal Inactivated Influenza Vaccines (2007), demonstrating non-inferior immunogenicity of a candidate vaccine compared to a US-licensed vaccine may support the use of the new vaccine in populations not included in the clinical endpoint efficacy study [FDA, 2007].

This study was designed to demonstrate non-inferiority of FLU Q-QIV compared to a US-licensed vaccine in children 6 to 35 months of age, which will serve as the pivotal evidence for licensure of FLU Q-QIV. *Fluzone Quadrivalent* was chosen as a comparator since it is currently the only QIV vaccine licensed in the US in children from 6 months old onwards.

To provide additional supportive evidence, the seroconversion rate (SCR) and seroprotection rate (SPR) for each strain of the FLU Q-QIV candidate were also evaluated against CBER's acceptance critera (lower limit 95% confidence interval [CI] for SCR $\geq$ 40% and lower limit 95% CI for SPR $\geq$ 70%).

Two 0.5 mL doses of FLU Q-QIV or two 0.25 mL doses of *Fluzone Quadrivalent* were administered intramuscularly (IM) at an approximate 28-day interval to children 6 to 35 months of age who were vaccine-unprimed. Vaccine-primed subjects received a single 0.5 mL dose of FLU Q-QIV or a single 0.25 mL dose of *Fluzone Quadrivalent.* Two blood samples were collected for haemagglutination inhibition (HI) antibody testing: the first on Day 0 (both vaccine-primed and -unprimed subjects) and the second on Day 28 (vaccine-primed subjects) or Day 56 (vaccine-unprimed subjects).

5.2. Study procedures

Table 1 and Table 2 summarize the list of study procedures during study visits and the final study contact for vaccine-primed and -unprimed subjects, respectively.

Table 1 List of study procedures for vaccine-primed subjects

Age	6 to 35 months		
Epoch	Epoch 001		
Type of contact	Visit 1	Visit 2	Site/Phone contact *
Time points	Day 0	Day 28	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	
Informed consent by parent(s)/LAR(s)	●		
Check inclusion/exclusion criteria	●		
Check elimination criteria		●	●
Collect demographic data (including weight and height)	●		
History of influenza vaccination ‡	●		
Medical history	●		
Physical examination	●	● §	
Check contraindications to vaccination	●		
Pre-vaccination body temperature	●		
Randomisation - Study group and treatment number allocation	●		
Blood sampling (approximately 4 mL) for humoral immune response determination	●	●	
Study vaccine administration	●		
30 minutes post-vaccination observation	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily (Days 0-6) and unsolicited AEs (Days 0-27)	O		
Return of diary cards		O	
Diary card transcription by investigator		●	
Record any concomitant medication/vaccination	●	●	●
Record any intercurrent medical conditions	●	●	●
Recording of SAEs	● #	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●
Recording of MAEs, pIMDs and events being considered for inclusion as potential risks in the RMP	●	●	●
Study conclusion			●

AE = adverse event; LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; pIMDs = potential Immune-Mediated Diseases; RMP = Risk Management Plan; SAE = Serious Adverse Event; Vacc = vaccination

● is used to indicate a study procedure that required documentation in the individual eCRF

○ is used to indicate a study procedure that did not require documentation in the individual eCRF

* Site Visit in case a subject preferred a visit instead of a phone contact.

‡ Recorded prior influenza vaccinations for the previous three influenza seasons (2013/2014, 2012/2013, 2011/2012), including the vaccine type (inactivated versus live intranasal).

§ if deemed necessary by the investigator.

Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

Table 2 List of study procedures for vaccine-unprimed subjects

Age	6 to 35 months			
Epoch	Epoch 001			
Type of contact	Visit 1	Visit 2	Visit 3	Site/Phone contact *
Time points	Day 0	Day 28	Day 56	Day 180
Sampling time points	Pre-Vacc	Post-Vacc 1	Post-Vacc 2	
Informed consent by parent(s)/LAR(s)	●			
Check inclusion/exclusion criteria	●			
Check elimination criteria (see Section 5.6.1)		●	●	●
Collect demographic data (including weight and height)	●			
History of influenza vaccination ‡	●			
Medical history	●			
Physical examination	●	● §	● §	
Check contraindications to vaccination	●	●		
Pre-vaccination body temperature	●	●		
Randomisation - Study group and treatment number allocation	●			
Treatment number allocation for subsequent doses		●		
Blood sampling (approximately 4 mL) for humoral immune response determination	●		●	
Study vaccine administration	●	●		
30 minutes post-vaccination observation	●	●		
Distribution of diary cards for post-vaccination recording of solicited AEs daily (Days 0-6) and unsolicited AEs (Days 0-27)	O	O		
Return of diary cards		O	O	
Diary card transcription by investigator		●	●	
Record any concomitant medication/vaccination	●	●	●	●
Record any intercurrent medical conditions	●	●	●	●
Recording of SAEs	● #	●	●	●
Recording of SAEs related to study participation or to a concurrent GSK medication/vaccine	● #	●	●	●
Recording of MAEs, pIMDs and events being considered for inclusion as potential risks in the RMP	●	●	●	●
Study conclusion				●

AE = adverse events; LAR = Legally Acceptable Representative; MAE = Medically Attended Adverse Event; pIMDs = potential Immune-Mediated Diseases; RMP = Risk Management Plan; SAE = Serious Adverse Event; Vacc = vaccination

● is used to indicate a study procedure that required documentation in the individual eCRF

○ is used to indicate a study procedure that did not require documentation in the individual eCRF

* Site Visit in case a subject preferred a visit instead of a phone contact.

‡ Recorded prior influenza vaccinations for the previous three influenza seasons (2013/2014, 2012/2013, 2011/2012), including the vaccine type (inactivated versus live intranasal).

§ if deemed necessary by the investigator.

Prior to vaccination, reporting was limited to fatal SAEs and SAEs related to study participation or administration of a GSK concomitant medication.

Table 3 Intervals between study visits in vaccine-primed subjects

Interval	Optimal length of interval [1]	Allowed interval [2]
Visit 1 (Day 0) → Visit 2 (Day 28)	28 days	25 - 42 days
Visit 1 (Day 0) → Site/Phone contact (Day 180)	180 days	166 - 201 days

[1] Whenever possible the investigator was to arrange study visits within this interval.

[2] Subjects were not eligible for inclusion in the According-To-Protocol (ATP) cohort for analysis of immunogenicity (see Section 5.10.5.3 for the definition) if they made the study visit outside this interval.

Table 4 Intervals between study visits in vaccine-unprimed subjects

Interval	Optimal length of interval [1]	Allowed interval [2]
Visit 1 (Day 0) → Visit 2 (Day 28)	28 days	25 -42 days
Visit 2 (Day 28) → Visit 3 (Day 56)	28 days	25 - 42 days
Visit 1 (Day 0) → Site/Phone contact (Day 180)	180 days	166 - 201 days

[1] Whenever possible the investigator was to arrange study visits within this interval.

[2] Subjects were not eligible for inclusion in the ATP cohort for analysis of immunogenicity (see Section 5.10.5.3 for the definition) if they made the study visit outside this interval.

5.3. Selection of study population

5.3.1. Inclusion criteria for enrolment

Deviations from inclusion criteria were not to be allowed because they could potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol was essential.

All subjects were to have satisfied ALL the following criteria at study entry:

- Subjects' parent(s)/Legally Acceptable Representative(s) [LAR(s)] who, in the opinion of the investigator, could and would comply with the requirements of the protocol (e.g. completion of the diary cards, return for follow-up visits).
- A male or female between, and including, 6 and 35 months of age at the time of the first vaccination.
- Written informed consent obtained from the parent(s)/LAR(s) of the subject.
- Subjects in stable health as determined by the investigator's clinical examination and assessment of the subjects' medical history.
- Subjects were eligible regardless of history of administration of influenza vaccine in a previous season.

5.3.2. Exclusion criteria for enrolment

Deviations from exclusion criteria were not to be allowed because they could potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol was essential.

The following criteria were to be checked at the time of study entry. If ANY exclusion criterion applies, the subject was not to have been included in the study:

- Use of any investigational or non-registered product (drug or vaccine) other than the study vaccine within 30 days preceding the first dose of study vaccine, or planned use during the study period. Routine registered childhood vaccinations are permitted.
- Child in care. Please refer to the GLOSSARY OF TERMS for the definition of child in care
- Chronic administration (defined as more than 14 days in total) of immunosuppressants or other immune-modifying drugs within six months prior to the first vaccine dose. For corticosteroids, this meant a dose equivalent to either > 2 mg/kg/day of body weight, or to ≥ 20 mg/day of prednisone for persons who weighed ≥ 10 kg, when administered for more than 2 weeks. Inhaled and topical steroids were allowed.
- Prior receipt of any seasonal or pandemic influenza vaccine (registered or investigational) within six months preceding the first dose of study vaccine, or planned use during the study period.
- Administration of immunoglobulins and/or any blood products within the three months preceding the first dose of study vaccine or planned administration during the study period.
- History of Guillain-Barré syndrome within six weeks of receipt of prior influenza vaccine.
- Any known or suspected allergy to any constituent of influenza vaccines (including egg proteins); a history of anaphylactic-type reaction to consumption of eggs; or a history of severe adverse reaction to a previous influenza vaccine.
- Acute disease and/or fever at the time of enrolment.
  - Fever was defined as temperature ≥38.0°C/100.4°F by any route.
  - Subjects with a minor illness (such as mild diarrhoea, mild upper respiratory infection) without fever could be enrolled at the discretion of the investigator.
- Any significant disorder of coagulation or treatment with warfarin derivatives or heparin.
- Any confirmed or suspected immunosuppressive or immunodeficient condition, based on medical history and physical examination (no laboratory testing required).
- Any other condition which, in the opinion of the investigator, prevented the subject from participating in the study.

5.3.3. Subject completion and withdrawal

5.3.3.1. Subject completion

A subject who returned for the concluding visit, or was available for the concluding contact foreseen in the protocol, was considered to have completed the study.

5.3.3.2. Subject withdrawal from the study

From an analysis perspective, a 'withdrawal' from the study referred to any subject who did not come back for the concluding visit/was not available for the concluding contact foreseen in the protocol.

All data collected until the date of withdrawal/last contact of the subject was to be used for the analysis.

A subject was considered a 'withdrawal' from the study when no study procedure had occurred, no follow-up had been performed and no further information had been collected for this subject from the date of withdrawal/last contact.

Investigators were to make an attempt to contact those subjects who do not return for scheduled visits or follow-up.

Subjects who were withdrawn because of SAEs/AEs were to be clearly distinguished from subjects who were withdrawn for other reasons. Investigators were to follow subjects who were withdrawn as result of SAE/AE until resolution of the event. Withdrawals were not to be replaced.

Information relative to the withdrawal was to be documented in the eCRF. The investigator was to document whether the decision to withdraw a subject from the study was made by the subject himself/herself, by the subject's parent(s) or LAR(s), or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- Serious adverse event.
- Non-serious adverse event.
- Protocol violation (specify).
- Consent withdrawal, not due to an adverse event*.
- Moved from the study area.
- Lost to follow-up.
- Other (specify).

*In case a subject was withdrawn from the study because he/she/the subject's parent(s) had withdrawn consent, the investigator was to document the reason for withdrawal of consent, if specified by the subject, in the CRF.

Subjects who were withdrawn from the study because of SAEs/AEs were to be clearly distinguished from subjects who were withdrawn for other reasons. Investigators were to follow subjects who were withdrawn from the study as result of a SAE/AE until resolution of the event.

5.3.3.3. Subject withdrawal from investigational vaccine

A 'withdrawal' from the investigational vaccine referred to any subject who did not receive the complete treatment, i.e. when no further planned dose was administered from the date of withdrawal. A subject withdrawn from the investigational vaccine may not have been necessarily withdrawn from the study as further study procedures or follow-up may have been performed (safety or immunogenicity) if planned in the study protocol.

Information relative to premature discontinuation of the investigational vaccine was to be documented on the Vaccine Administration screen of the eCRF. The investigator was to document whether the decision to discontinue further vaccination/treatment was made by the subject himself/herself, by the subject's parent(s) or LAR(s), or by the investigator, as well as which of the following possible reasons was responsible for withdrawal:

- Serious adverse event.
- Non-serious adverse event.
- Other (specify).

5.3.3.4. Contraindications to subsequent vaccination

The following events constituted absolute contraindications to further administration of the study vaccine. If any of these events occurred during the study, the subject was not to have received additional doses of vaccine but may have continued other study procedures at the discretion of the investigator.

- Anaphylaxis following the administration of vaccine(s).

The following events constituted contraindications to administration of the study vaccine at that point in time; if any of these events occurred at the time scheduled for vaccination, the subject may have been vaccinated at a later date, within the time window specified in the protocol, or the subject may have been withdrawn at the discretion of the investigator.

- Acute disease and/or fever at the time of vaccination.
  - Acute disease was defined as the presence of a moderate or severe illness with or without fever.
  - Fever was defined as temperature ≥ 38.0°C/100.4°F by any route.
  - Subjects with a minor illness (such as mild diarrhea, mild upper respiratory infection) without fever could have been vaccinated.

5.4. Composition and administration of vaccine(s)

5.4.1. Description of vaccines

GSK Biologicals' quadrivalent split virion influenza vaccine 2014/2015 was composed of inactivated viral fragments of 4 distinct strains of influenza virus (total antigen HA content of 60 µg, i.e., 15 µg/strain) selected in accordance with World Health Organization (WHO) recommendation (20 February 2014) that the virus strains for use in

the 2014-2015 Northern Hemisphere influenza season should remain the same as those in the 2013-2014 vaccine[WHO, 2014]. This was also the recommendation of FDA's CBER, and the European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use (CHMP). The *Fluzone Quadrivalent* vaccine also contained the same 4 WHO-recommended strains, but with a total antigen HA content of 30 µg (i.e., 7.5 µg/strain).

Specific information about the study vaccines, including strain formulation, presentation, and excipients, is provided in Table 5. The excipients used in the FLU Q-QIV and *Fluzone Quadrivalent* formulations comply with the US and/or European Pharmacopoeia.

The Quality Control Standards and Requirements for the vaccine were described in separate Quality Assurance documents (e.g. release protocols, certificate of analysis) and the required approvals had been obtained. The vaccines were labeled and packed according to applicable regulatory requirements. The commercial vaccine, *Fluzone Quadrivalent,* was assumed to comply with the specifications given in the manufacturer's Summary of Product Characteristics.

While the FLU Q-QIV-022 study was still ongoing in the extended safety follow-up period following completion of the active vaccination phase, it was observed that two out of the three representative lots for FluLaval Quadrivalent Thimerosal-Free Pre-Filled Syringes (Q-QIV TF PFS) being monitored in a commercial stability program experienced Out of Specification (OOS) results for potency of HA content (µg/mL as measured by the Single Radial Immunodiffusion [SRID] assay). These OOS results were observed for B/Massachusetts/2/2012 strain and for B/Brisbane/60/2008 strain where the observed reduction in potency below the specified minimum was minimal.

Although the particular Q-QIV PFS lot used in the FLU Q-QIV-022 study was not tested, the 3 tested lots are considered representative of all FluLaval® Quadrivalent Influenza vaccine in pre-filled syringes. Since a reduction in potency below the specified minimum could reduce the immune response elicited by Q-QIV, the remaining doses of commercial Q-QIV TF were recalled.

Since the active vaccination phase of the study had been completed when the OOS result became available, it was decided in consultation with study IRBs to continue the safety follow up as specified in the protocol. A "Dear Investigator" letter and communication template for parents/LARs were provided to all study Investigators who were then requested to decide, in conjunction with their respective IRB, the best way to communicate the information to the parents/LARs.

Table 5 Study vaccines

Treatment name	Vaccine name	Formulation	Excipients	Presentation	Volume	Number of doses
Q-QIV	FLU-Q-QIV	A/California/07/2009(H1N1)=15µg; A/Texas/50/2012(H3N2)=15µg; B/Massachusetts/2/2012=15µg; B/Brisbane/60/2008=15µg	Sodium chloride, potassium chloride, sodium phosphate dibasic heptahydrate, potassium phosphate monobasic, alpha-tocopheryl hydrogen succinate, polysorbate 80 (Tween 80) and water for injection	Translucent to whitish opalescent suspensions that may sediment slightly, presented in prefilled syringes	0.5 ml	1 (vaccine-primed subjects) 2 (vaccine-unprimed subjects)
F-QIV	*Fluzone quadrivalent*	A/California/07/2009(H1N1)=7.5µg; A/Texas/50/2012(H3N2)=7.5µg; B/Massachusetts/2/2012=7.5µg; B/Brisbane/60/2008=7.5µg	Sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde, octylphenol ethoxylate	Clear and slightly opalescent presented in prefilled syringes	0.25 ml	1 (vaccine-primed subjects) 2 (vaccine-unprimed subjects)

Q-QIV = FLU Q-QIV
F-QIV = *Fluzone Quadrivalent*

5.4.2. Dosage and administration of study vaccines

Vaccine-primed subjects were to receive a single 0.5 mL dose of FLU Q-QIV or a single 0.25 mL dose of *Fluzone Quadrivalent* administered IM on Day 0. Vaccine-unprimed subjects were to receive two 0.5 mL doses of FLU Q-QIV or two 0.25 mL doses of *Fluzone Quadrivalent* administered IM on Days 0 and 28.

- The vaccines were to be administered into the anterolateral region of the thigh (subjects below 12 months of age) or in the deltoid region (subjects ≥12 months of age). The buttock was not to be used for administration of vaccines because of the potential risk of injury to the sciatic nerve and the risk of decreased immunogenicity because of inadvertent subcutaneous injection or injection into deep fat tissue.
- The injection needle used in the intramuscular administration of the vaccine was to be long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underling nerves and blood vessels or bone. For injection into either the deltoid muscle or anterolateral region of the thigh, a 25 mm (1 inch), 22-25 gauge needle is typical. Although it was recommended to follow this guideline, an individual decision on needle size and site of injection was to be made for each person on the basis of age and muscle size. Vaccinators were to be familiar with the anatomy of the area into which they are injecting vaccine.

The vaccinees were to be observed closely for at least 30 minutes following administration of the vaccine, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

The vaccines were to be administered as described below for subjects <12 months of age (Table 6) and for subjects ≥12 months of age (Table 7).

Table 6 Dosage and administration for subjects below 12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route	Site [1]	Side
Visit 1 (Day 0)	0.5 ml	Q-QIV PRIM	Q-QIV	IM	Anterolateral thigh	Left
Visit 1 (Day 0)		Q-QIV UNPRIM				
Visit 2 (Day 28)		Q-QIV UNPRIM				
Visit 1 (Day 0)	0.25 ml	F-QIV PRIM	F-QIV	IM	Anterolateral thigh	Left
Visit 1 (Day 0)		F-QIV UNPRIM				
Visit 2 (Day 28)		F-QIV UNPRIM				

[1]Thigh injection is the recommended route for subjects < 12 months, however the other route (deltoid) might be considered based on a subject's individual anatomy.
IM = intramuscular; PRIM = Vaccine-primed subjects; UNPRIM = Vaccine-unprimed subjects

Table 7 Dosage and administration for subjects >=12 months of age

Type of contact and time point	Volume to be administered	Study group	Treatment name	Route	Site [1]	Side [2]
Visit 1 (Day 0)	0.5 ml	Q-QIV PRIM	Q-QIV	IM	Deltoid	Non-dominant
Visit 1 (Day 0)		Q-QIV UNPRIM				
Visit 2 (Day 28)		Q-QIV UNPRIM				
Visit 1 (Day 0)	0.25 ml	F-QIV PRIM	F-QIV	IM	Deltoid	Non-dominant
Visit 1 (Day 0)		F-QIV UNPRIM				
Visit 2 (Day 28)		F-QIV UNPRIM				

[1]Deltoid injection is the recommended route for subjects ≥ 12 months, however the other route (thigh) might be considered based on a subject's individual anatomy.
[2]Or left arm if dominance is not yet identified.
IM = intramuscular; PRIM = Vaccine-primed subjects; UNPRIM = Vaccine-unprimed subjects

5.4.3. Treatment allocation and randomization

Subject identification numbers were assigned sequentially to the subjects who had consented to participate in the study, according to the range of subject identification numbers allocated to each study center.

The randomization of supplies within blocks were performed at GSK Biologicals, using MATerial EXcellence (MATEX), a program developed for use in Statistical Analysis System (SAS®) (Cary, NC, USA) by GSK Biologicals. Entire blocks were shipped to the study centers /warehouse(s).

To allow GSK Biologicals to take advantage of greater rates of recruitment than anticipated at individual centers in this multi-center study and to thus reduce the overall study recruitment period, an over-randomization of supplies was to be prepared.

The treatment numbers were allocated by dose. Each dose was to have a single unique treatment number throughout the study. Eligible subjects were randomized in a 1:1 ratio to receive either FLU Q-QIV or *Fluzone Quadrivalent*. The target was to enroll approximately 2400 eligible subjects who were to be randomly assigned to the 2 study groups in a 1:1 ratio (approximately 1200 subjects in each group). The randomization algorithm used a minimization procedure accounting for age (6-17 and 18-35 months), study center, and the pre-study influenza vaccine priming status of the subjects to ensure balanced representation of the combination of the minimization factors in the two study groups. The study aimed to enroll at least 40%, but no more than 50%, of the total subjects in the age group of 6-17 months of age.

Allocation of the subject to a study group at the investigator site was performed using a randomization system on internet (SBIR).

After obtaining the signed and dated ICF/IAF (as applicable) from the subject and having checked the eligibility of the subject, the site staff in charge of the vaccine administration, were to access SBIR. Upon providing the subject identification number, the randomization system would have determined the study group and provided the treatment number to be used for each dose.

For each dose subsequent to the first dose, the study staff in charge of the vaccine administration were to access SBIR, provide the subject identification number, and the system would have provided a treatment number consistent with the allocated study group.

The number of each administered treatment was to be recorded in the eCRF on the Vaccine Administration screen.

5.5. Blinding

Data was to be collected in an observer-blind manner. By observer-blind, it is meant that during the course of the study, the subject, subject‘s parent(s)/LAR(s), and those responsible for the evaluation of any study endpoint (e.g. safety, reactogenicity) were all to be unaware of the treatment assignments. Therefore, vaccine preparation and administration were be done by authorized medical personnel who were not to participate in any of the study clinical evaluation assays.

The laboratory in charge of the laboratory testing was to be blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

5.6. Prior and concomitant medication /vaccinations

The following concomitant medications/products/vaccines were to be recorded in the eCRF if administered during the indicated recording period:

- All concomitant medications/products, except vitamins and dietary supplements, administered starting 30 days before the first dose of study vaccine and for 28 days following each dose of study vaccine.
- Prophylactic medication (i.e. medication administered in the absence of ANY symptom and in anticipation of a reaction to the vaccination) had to be recorded as from 2 days before administration of the study vaccine to 28 days after the last dose of study vaccine.
  - E.g., an anti-pyretic was considered to be prophylactic when it was given in the absence of fever and any other symptom, to prevent fever from occurring [fever is defined as temperature ≥ 38.0°C/100.4°F by any route].
- Any concomitant vaccination administered in the period starting 30 days before the first dose of study vaccine and ending at the last study contact.
- Any influenza vaccine within up to 6 months before the administration of study vaccine on Day 0 or at any time from Day 0 to study end.
- Any investigational medication or vaccine administered in the period starting 30 days before the administration of the study vaccine until the end of the study.
- Any concomitant medications/products/vaccines listed in Section 5.6.1.
- Any concomitant medication/product/vaccine relevant to a SAE*/pIMD or administered at any time during the study period for the treatment of a SAE*/pIMD (*SAEs that are required to be reported per protocol).

5.6.1. Concomitant medications/products/vaccines that may have led to the elimination of a subject from ATP analyses

The use of the following concomitant medications/products/vaccines did not require withdrawal of the subject from the study but may have determined a subject's evaluability in the ATP analysis.

- Any investigational or non-registered product (drug or vaccine) other than the study vaccine(s) used during the study period.
- Administration of influenza vaccines other than the study vaccines during the study period.
- Immunosuppressants or other immune-modifying drugs administered chronically (i.e. more than 14 days) during the study period. For corticosteroids, this meant a dose equivalent to either > 2 mg/kg/day of body weight, or to ≥ 20 mg/day of prednisone for persons who weigh ≥ 10 kg, when administered for more than 2 weeks. Inhaled and topical steroids were allowed.
- Immunoglobulins and/or any blood products administered during the study period.

5.7. Intercurrent medical conditions that may have lead to elimination of a subject from ATP analyses

Subjects may have been eliminated from the ATP cohort for immunogenicity if, during the study, they incurred a condition that had the capability of altering their immune response (i.e. any confirmed or suspected immunosuppressive or immunodeficient condition based on medical history and physical examination (no laboratory testing required).

5.8. Assessment of immunogenicity variables

Serological assays for the measurement of HI antibody titers were performed at a GSK Biologicals' laboratory or in a laboratory designated by GSK Biologicals using standardized and validated procedures (Table 8). Total blood volume to be taken from each subject over the study period was approximately 8.0 mL (2 time points x 4.0 mL).

Table 8 Humoral Immunity (Antibody determination)

System	Component	Method	Kit/ Manufacturer	Unit	Cut-off	Laboratory
Serum	Influenza Virus A/California/7/2009 (H1N1).Hemagglutinin Ab*	HAI	In-house assay (GSK)	1/DIL	10	GSK Biologicals**
Serum	Influenza Virus A/Texas/50/2012 (H3N2).Hemagglutinin Ab*	HAI	In-house assay (GSK)	1/DIL	10	GSK Biologicals**
Serum	Influenza Virus B/Brisbane/60/2008 (Victoria).Hemagglutinin Ab*	HAI	In-house assay (GSK)	1/DIL	10	GSK Biologicals**
Serum	Influenza Virus B/Massachusetts/2/2012 (Yamagata).Hemagglutinin Ab*	HAI	In-house assay (GSK)	1/DIL	10	GSK Biologicals**

1/DIL = 1/dilution; H(A)I = Haemagglutination Inhibition

*The strains included in *Fluzone Quadrivalent* and FLU Q-QIV were in accordance with WHO recommendations for the Northern Hemisphere – Season 2014/2015.

**GSK Biologicals laboratory refers to the Global Vaccines Clinical Laboratories (GVCL) in Rixensart, Belgium; Wavre, Belgium; Laval, Canada; or Dresden, Germany.

The GSK Biologicals' clinical laboratories have established a Quality System supported by procedures. The activities of GSK Biologicals' clinical laboratories are audited regularly for quality assessment by an internal (sponsor-dependent) but laboratory-independent Quality Department.

5.8.1. Immunological read-outs

Table 9 Immunological read-outs

Blood sampling time point		Subset Name	No. subjects	Component
Type of contact and time point	Sampling time point			
Visit 1 (Day 0)	Pre-Vacc	All subjects	2400	4 strains*
Visit 2 (Day 28)	Post-Vacc 1	Vaccine-primed subjects	Max 2400	4 strains*
Visit 3 (Day 56)	Post-Vacc 2	Vaccine-unprimed subjects	Max 2400	4 strains*

5.8.2. Immunological correlates of protection

Although no generally accepted immunological correlate of protection has been demonstrated so far against influenza (either seasonal or pandemic) with respect to specific levels of HI-specific antibody titer post-vaccination induced with inactivated influenza virus vaccines, the protective role of antibodies against haemagglutinin and, to a lesser extent, neuraminidase, is well established and has been demonstrated both in experimentally infected animals and humans [Brydak, 2000, Rimmelzwaan, 2008].

For this reason, the induction of HA-specific antibodies is used as a marker of potential vaccine efficacy and the serum HI assay is used to demonstrate this humoral response. HI antibody titers of 1:40 or greater have been associated with protection from influenza illness in at least 50% of adult subjects in some human challenge studies [Hannoun, 2004; Hobson, 1972]. While the 1:40 titer is termed “seroprotection” for convenience, it is recognised that no association of this titer with protection has been formally demonstrated in children.

5.9. Assessment of safety variables

The standard definitions and reporting periods for AE and SAEs are provided in the Protocol.

5.9.1. Solicited adverse events

Solicited AEs (Table 10 and Table 11) occurring during the 7-day follow-up period after vaccination (day of vaccination and subsequent 6 days) were to be recorded in the appropriate section of the eCRF.

5.9.1.1. Solicited local (injection-site) adverse events

The following local (injection-site) AEs were solicited:

Table 10 Solicited local adverse events

Pain at the injection site
Redness at injection site
Swelling at injection site

5.9.1.2. Solicited general adverse events

The following general AEs were solicited:

Table 11 Solicited general adverse events

Drowsiness
Fever
Irritability/Fussiness
Loss of appetite

Note: Temperature was to be recorded in the evening. If additional temperature measurements were performed at other times of day, the highest temperature was to be recorded in the eCRF.

5.9.2. Clinical laboratory parameters and other abnormal assessments qualifying as adverse events or serious adverse events

In the absence of diagnosis, abnormal laboratory findings (e.g. clinical chemistry, hematology, urinalysis) or other abnormal assessments that were judged by the investigator to be clinically significant were to be recorded as AE or SAE if they met the definition of an AE or SAE. Clinically significant abnormal laboratory findings or other abnormal assessments that were present at baseline and significantly worsened following the start of the study were also be reported as AEs or SAEs. However, clinically significant abnormal laboratory findings or other abnormal assessments that were associated with the disease being studied, unless judged by the investigator as more severe than expected for the subject's condition, or that were present or detected at the start of the study and did not worsen, were not to be reported as AEs or SAEs.

The investigator was to exercise his or her medical and scientific judgement in deciding whether an abnormal laboratory finding or other abnormal assessment was clinically significant.

5.9.3. Adverse events of specific interest

5.9.3.1. Potential immune-mediated diseases

Potential immune-mediated diseases are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. AEs that needed to be recorded and reported as pIMDs include those listed in Table 12.

However, the investigator will exercise his/her medical and scientific judgement in deciding whether other diseases have an autoimmune origin (i.e. pathophysiology involving systemic or organ-specific pathogenic autoantibodies) and should also be recorded as a pIMD.

Table 12 List of potential immune-mediated diseases

Neuroinflammatory disorders	Musculoskeletal disorders	Skin disorders
• Cranial nerve disorders, including paralyses/paresis (e.g. Bell's palsy) • Optic neuritis • Multiple sclerosis • Transverse myelitis • Guillain-Barré syndrome, including Miller Fisher syndrome and other variants • Acute disseminated encephalomyelitis, including site specific variants: e.g. non-infectious encephalitis, encephalomyelitis, myelitis, myeloradiculoneuritis • Myasthenia gravis, including Lambert-Eaton myasthenic syndrome • Immune-mediated peripheral neuropathies and plexopathies, (including chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy). • Narcolepsy	• Systemic lupus erythematosus and associated conditions • Systemic scleroderma (Systemic sclerosis), including diffuse systemic form and CREST syndrome Idiopathic inflammatory myopathies, including dermatomyositis • Polymyositis • Antisynthetase syndrome • Rheumatoid arthritis, and associated conditions including juvenile chronic arthritis and Still's disease • Polymyalgia rheumatica • Spondyloarthritis, including ankylosing spondylitis, reactive arthritis (Reiter's Syndrome) and undifferentiated spondyloarthritis • Psoriatic arthropathy • Relapsing polychondritis • Mixed connective tissue disorder	• Psoriasis • Vitiligo • Erythema nodosum • Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis) • Alopecia areata • Lichen planus • Sweet's syndrome • Localised Scleroderma (Morphoea)
Vasculitides	**Blood disorders**	**Others**
• Large vessels vasculitis including: giant cell arteritis such as Takayasu's arteritis and temporal arteritis. • Medium sized and/or small vessels vasculitis including: polyarteritis nodosa, Kawasaki's disease, microscopic polyangiitis, Wegener's granulomatosis, Churg–Strauss syndrome (allergic granulomatous angiitis), Buerger's disease (thromboangiitis obliterans), necrotizing vasculitis and anti-neutrophil cytoplasmic antibody (ANCA) positive vasculitis (type unspecified), Henoch-Schonlein purpura, Behcet's syndrome, leukocytoclastic vasculitis.	• Autoimmune hemolytic anemia • Autoimmune thrombocytopenia • Antiphospholipid syndrome • Pernicious anemia • Autoimmune aplastic anaemia • Autoimmune neutropenia • Autoimmune pancytopenia	• Autoimmune glomerulonephritis (including IgA nephropathy, glomerulonephritis rapidly progressive, membranous glomerulonephritis, membranoproliferative glomerulonephritis, and mesangioproliferative glomerulonephritis) • Ocular autoimmune diseases (including autoimmune uveitis and autoimmune retinopathy) • Autoimmune myocarditis/cardiomyopathyS arcoidosis • Stevens-Johnson syndrome • Sjögren's syndrome • Idiopathic pulmonary fibrosis • Goodpasture syndrome • Raynaud's phenomenon
Liver disorders	**Gastrointestinal disorders**	**Endocrine disorders**
• Autoimmune hepatitis • Primary biliary cirrhosis • Primary sclerosing cholangitis	• Inflammatory Bowel disease, including Crohn's disease, ulcerative colitis,	• Autoimmune thyroiditis (including Hashimoto thyroiditis)

Neuroinflammatory disorders	Musculoskeletal disorders	Skin disorders
• Autoimmune cholangitis	microscopic colitis, ulcerative proctitis • Celiac disease • Autoimmune pancreatitis	• Grave's or Basedow's disease • Diabetes mellitus type I • Addison's disease • Polyglandular autoimmune syndrome • Autoimmune hypophysitis

When there was enough evidence to make any of the above diagnoses, the AE had to be reported as a pIMD. Symptoms, signs or conditions which might (or might not) have represented the above diagnoses, should have been recorded and reported as AEs but not as pIMDs until the final or definitive diagnosis had been determined, and alternative diagnoses had been eliminated or shown to be less likely.

In order to facilitate the documentation of pIMDs in the eCRF, a pIMD standard questionnaire and a list of preferred terms (PTs) and PT codes corresponding to the above diagnoses were made available to investigators at study start.

5.9.3.2. Potential risks in the Risk Management Plan (RMP)

The AEs below were being considered for inclusion in the RMP for FLU Q-QIV as potential risks. Therefore, the AEs were to be closely monitored through the entire study period and reported as SAEs. The parent(s)/LAR(s) were to be instructed to report these events to the investigator immediately. The investigator was to report the event(s) to GSK Biologicals within 24 hours once the investigator was aware of the event:

- Anaphylaxis
- Febrile seizure
- Bell's palsy
- Guillain-Barré syndrome
- Injection site haemorrhage in individuals with thrombocytopenia or any other coagulation disorder
- Narcolepsy

5.9.4. Time period for detecting and recording adverse events and serious adverse events

All AEs starting within the time frame specified were to be recorded into the appropriate section of the eCRF, irrespective of intensity or whether or not they were considered vaccination-related. Specifically, in the United States, all AEs starting within 28 days following administration of each dose of study vaccine/comparator had to be recorded into the appropriate section of the eCRF. In Mexico, all AEs during the entire study period, i.e., from Day 0 to Day 180, had to be recorded into the appropriate section of the eCRF to comply with local regulations.

The time period for collecting and recording SAEs began at the first receipt of study vaccine/comparator and ended on the day of study conclusion.

All AEs/SAEs leading to withdrawal from the study were collected and recorded from the time of the first receipt of study vaccine/comparator until the end of the study for each subject.

In addition to the above-mentioned reporting requirements and in order to fulfill international reporting obligations, SAEs that were related to study participation (i.e. protocol-mandated procedures, invasive tests, a change from existing therapy) or were related to a concurrent GSK medication/vaccine were to be collected and recorded from the time the subject's parent(s)/LAR(s) consented to allow the subject to participate in the study until the subject was discharged from the study.

The time period for collecting and recording of MAEs, pIMDs and the events being considered for inclusion as potential risks in the FLU Q-QIV RMP began at the first receipt of study vaccine/comparator and ended at study conclusion for each subject.

A post-study AE/SAE was defined as any event that occurred outside of the AE/SAE reporting period defined. Investigators were not obligated to actively seek AEs or SAEs in former study participants. However, if the investigator learnt of any SAE at any time after a subject had been discharged from the study, and he/she considered the event reasonably related to the investigational vaccine/product, the investigator was to promptly notify the Study Contact for Reporting SAEs.

An overview of the protocol-required reporting periods for AEs and SAEs, is given in Table 13 (for the United States) and Table 14 (for Mexico).

Table 13 Reporting periods (in the United States) for adverse events and serious adverse events

Event	Pre-Vacc*		Vacc 1	7 days post-Vacc 1	28 days post-Vacc 1		Vacc 2**	7 days post-Vacc 2**	28 days post-Vacc 2**		6 months post-Vacc 1
Time point			**Day 0**	**Day 6**	**Day 27**		**Day 28**	**Day 34**	**Day 56**		**Day 180**
Solicited local and general AEs											
§Unsolicited AEs											
AEs/SAEs leading to withdrawal from the study											
SAEs related to study participation or concurrent GSK medication/vaccine											
SAEs, events being considered for inclusion as potential risks in the RMP, MAEs and pIMDs											
Recording of intercurrent medical conditions											

Vacc = vaccination; Pre-Vacc = pre-vaccination
*Informed consent obtained
**Only for vaccine-unprimed subject
§For the United States, unsolicited AEs were to be collected from Day 0 to Day 27 after each vaccination

Table 14 Reporting periods (in Mexico) for adverse events and serious adverse events

Event	Pre-Vacc*		Vacc 1	7 days post-Vacc 1	28 days post-Vacc 1		Vacc 2**	7 days post-Vacc 2**	28 days post-Vacc 2**		6 months post-Vacc 1
Time point			**Day 0**	**Day 6**	**Day 27**		**Day 28**	**Day 34**	**Day 56**		**Day 180**
Solicited local and general AEs											
§Unsolicited AEs											
AEs/SAEs leading to withdrawal from the study											
SAEs related to study participation or concurrent GSK medication/vaccine											
SAEs, events being considered for inclusion as potential risks in the RMP, MAEs and pIMDs											
Recording of intercurrent medical conditions											

Vacc = vaccination; Pre-Vacc = pre-vaccination
*Informed consent obtained
**Only for vaccine-unprimed subject
§For Mexico, unsolicited AEs were to be collected for the entire duration of the study (Day 0 to Day 180)

5.9.5. Assessment of adverse events

5.9.5.1. Assessment of intensity

The intensity of the following solicited AEs was to be assessed as described:

Table 15 Intensity scales for solicited symptoms in infants/toddlers and children

Infant/Toddler (15–24 months)/Child		
Adverse Event	Intensity grade	Parameter
Pain at injection site	0	None
	1	Mild: Minor reaction to touch
	2	Moderate: Cries/protests on touch
	3	Severe: Cries when limb is moved/spontaneously painful
Redness at injection site		Record greatest surface diameter in mm
Swelling at injection site		Record greatest surface diameter in mm
Fever*		Record temperature in °C/°F
Irritability/Fussiness	0	Behaviour as usual
	1	Mild: Crying more than usual/no effect on normal activity
	2	Moderate: Crying more than usual/interferes with normal activity
	3	Severe: Crying that cannot be comforted/prevents normal activity
Drowsiness	0	Behaviour as usual
	1	Mild: Drowsiness easily tolerated
	2	Moderate: Drowsiness that interferes with normal activity
	3	Severe: Drowsiness that prevents normal activity
Loss of appetite	0	Appetite as usual
	1	Mild: Eating less than usual/no effect on normal activity
	2	Moderate: Eating less than usual/interferes with normal activity
	3	Severe: Not eating at all

*Fever was defined as temperature ≥ 38.0°C / 100.4°F by any route.

The maximum intensity of local injection site redness/swelling was scored at GSK Biologicals as follows in Pediatric cohorts:

1 : > 20 - ≤ 50 mm
2 : > 50 - ≤ 100 mm
3 : > 100 mm

The maximum intensity of fever (defined as temperature ≥ 38.0°C/100.4°F by any route) was scored at GSK Biologicals as follows:

1 : ≥ 38.0°C (100.4°F) - ≤ 38.5°C (101.3°F)
2 : > 38.5°C (101.3°F) - ≤ 39.0°C (102.2°F)
3 : > 39.0°C (102.2°F) - ≤ 40.0°C (104°F)
4 : > 40.0°C (104°F)

The investigator was to assess the maximum intensity that occurred over the duration of the event for all unsolicited AEs (including SAEs) recorded during the study. The assessment was to be based on the investigator's clinical judgement.

The intensity was to be assigned to 1 of the following categories:

1 (mild)	=	An AE which was easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE which was sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE which prevented normal, everyday activities (in a young child, such an AE would, for example, have prevented attendance at school/kindergarten/a day-care center and would have caused the parent(s)/LAR(s) to seek medical advice)

An AE that was assessed as Grade 3 (severe) was not to be confused with a SAE. Grade 3 was a category used for rating the intensity of an event; and both AEs and SAEs can have been assessed as Grade 3. An event was defined as 'serious' when it met 1 of the pre-defined outcomes.

5.9.5.2. Assessment of causality

The investigator was obligated to assess the relationship between the investigational vaccine and the occurrence of each AE/SAE. The investigator was to use clinical judgement to determine the relationship. Alternative plausible causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational vaccine/product were to be considered and investigated. The investigator was also required to consult the IB and/or PI for marketed products to determine his/her assessment.

There might have been situations when a SAE had occurred and the investigator had minimal information to include in the initial report to GSK Biologicals. However, it was very important that the investigator always made an assessment of causality for every event prior to submission of the SAE report to GSK Biologicals. The investigator might have changed his/her opinion of causality in light of follow-up information and updated the SAE information accordingly. The causality assessment was 1 of the criteria used when determining regulatory reporting requirements.

In case of concomitant administration of multiple vaccines, it might not have been possible to determine the causal relationship of general AEs to the individual vaccines administered. The investigator was to have assessed whether the AE could have been causally related to vaccination rather than to the individual vaccines.

All solicited local (injection site) reactions were to be considered causally related to vaccination. Causality of all other AEs were to be assessed by the investigator using the following question:

Was there a reasonable possibility that the AE may have been caused by the investigational vaccine?

YES : There was a reasonable possibility that the vaccine(s) contributed to the AE.

NO : There was no reasonable possibility that the AE was causally related to the administration of the study vaccine(s). There were other, more likely causes and administration of the study vaccine(s) was not suspected to have contributed to the AE.

The definitions for 'NO' and 'YES' have been written in such a way that all events that were attributed a 'NO' can be pooled with events which in the past studies were determined to be 'not related' or 'unlikely to be related' to vaccination. Those events that were attributed a 'YES' can be pooled with those events that in the past were determined to have a 'suspected' or 'probable' relationship to vaccination in the primary vaccination study.

If an event met the criteria to be determined as 'serious', additional examinations/tests were to be performed by the investigator in order to determine ALL possible contributing factors for each SAE.

Possible contributing factors included:

- Medical history.
- Other medication.
- Protocol required procedure.
- Other procedure not required by the protocol.
- Lack of efficacy of the vaccine(s), if applicable.
- Erroneous administration.
- Other cause (to be specified).

5.9.5.3. Assessment of outcomes

The investigator was to assess the outcome of all unsolicited AEs (including SAEs) recorded during the study as:

- Recovered/resolved.
- Recovering/resolving.
- Not recovered/not resolved.
- Recovered with sequelae/resolved with sequelae.
- Fatal (SAEs only).

5.9.5.4. Medically attended visits

For each solicited and unsolicited symptom the subject experienced, the subject's parent(s)/LAR(s) was to be asked if the subject received medical attention defined as

hospitalization, or an otherwise unscheduled visit to or from medical personnel for any reason, including emergency room visits. This information was to be recorded in the eCRF.

5.9.6. Follow-up of adverse events and serious adverse events

5.9.6.1. Follow-up during the study

After the initial AE/SAE report, the investigator was required to proactively follow each subject and provide additional relevant information on the subject's condition to GSK Biologicals (within 24 hours for SAEs).

All SAEs, events being considered for inclusion as potential risks in the RMP, MAEs and pIMDs (serious or non-serious) documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were to be reviewed at subsequent visits/contacts until the end of the study.

With the exception of SAEs, events being considered for inclusion as potential risks in the RMP, MAEs and pIMDs, all AEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were to be reviewed at subsequent visits/contacts until 28 days after the last vaccination.

5.9.6.2. Follow-up after the subject is discharged from the study

The investigator was to follow subjects:

- With SAEs, events being considered for inclusion as potential risks in the RMP, pIMDs (serious or non-serious), or subjects withdrawn from the study as a result of an AE, until the event has resolved, subsided, stabilised, disappeared, or until the event is otherwise explained, or the subject is lost to follow-up.
- With MAEs, until the end of the study or the subjects are lost to follow-up.
- With other non-serious AEs, until Day 28 (vaccine-primed subjects) or Day 56 (vaccine-unprimed subjects) or they are lost to follow-up.

If the investigator received additional relevant information on a previously reported SAE, he/she was to provide this information to GSK Biologicals using a paper SAE and/or pregnancy report as applicable.

GSK Biologicals might have requested that the investigator perform or arrange the conduct of additional clinical examinations/tests and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE or SAE. The investigator was obliged to assist. If a subject died during participation in the study or during a recognized follow-up period, GSK Biologicals was to be provided with any available post-mortem findings, including histopathology.

5.10. Statistical methods

5.10.1. Primary endpoints

- Humoral immune response to each strain. Serum HI antibody titers for the four strains 28 days after the last vaccine dose was used to calculate
  - GMT ratio (*Fluzone Quadrivalent*/FLU Q-QIV)
  - SCR difference (*Fluzone Quadrivalent* minus FLU Q-QIV)

5.10.2. Secondary endpoints

- Humoral immune response to each strain, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed). Serum HI antibody on Day 0 and/or 28 days after the last vaccine dose from both groups will be used to calculate:
  - GMTs on Day 0 and 28 days after the last vaccine dose
  - SPRs on Day 0 and 28 days after the last vaccine dose
  - SCRs 28 days after the last vaccine dose
  - MGIs 28 days after the last vaccine dose
- Solicited local and general AEs, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed):
  - Occurrence of solicited local and general AEs (summarized by incidence rate, intensity, duration and relationship to vaccination [general AEs]) during a 7-day follow-up period (i.e. day of vaccination and six subsequent days) after each vaccination, in each group
- Unsolicited AEs, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed)
  - Occurrence of unsolicited AEs (summarized by incidence rate, intensity, and relationship to vaccination) during a 28-day follow-up period (i.e. day of vaccination and 27 subsequent days), in each group
- SAEs, MAEs, and pIMDs, overall, by age group (6-17 and 18-35 months of age) and by priming status (vaccine-primed and vaccine-unprimed
  - Occurrence of SAEs, MAEs and pIMDs (summarized by incidence rate and relationship) during the entire study period
- Occurrence of any fever (≥ 38°C) or Grade 3 fever or higher (> 39°C) during a 2-day follow-up period (i.e. day of vaccination and one subsequent day) after each vaccination

5.10.3. Exploratory endpoint

- Humoral immune responses measured by ELISA, other immunoassay formats or functional assays such as a virus neutralization test or a neuraminidase-inhibition test to assess the anti-influenza virus antibody responses elicited by vaccination depending on samples and testing availability.

5.10.4. Determination of sample size

The primary study objective to be powered was the immunogenic non-inferiority of FLU Q-QIV versus *Fluzone Quadrivalent* (in terms of GMT ratio and SCR difference) approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for vaccine-primed and -unprimed subjects, respectively) in the overall population.

Assuming a GMT ratio of 1.0 and an SCR difference of 0%, it was determined that 1020 evaluable subjects per group would be needed to achieve a global statistical power of 99% (Table 16).

Table 16 Statistical power needed to infer non-inferiority in terms of SCR and GMT ratio between FLU Q-QIV and *Fluzone Quadrivalent*

Endpoint	Non-inferiority criteria	Assumptions*	N1=N2 (evaluable)	Power for 1 strain	Power for 4 strains**
GMT Ratio	UL of 95% CI for GMT ratio ≤ 1.5	Log(SD) = 0.59	1020	>0.9999***	>0.9999
SCR Difference	UL of 95% CI for SCR difference ≤ 10%	SCR = 66.4%	1020	0.9977****	0.9908
Overall Power					**99.07%**

UL = upper limit; SD = standard deviation
*Based on results from FLU Q-QIV-021 (Q-QIV group), type I error = 2.5%.
**Using Bonferonni adjustment on Type II error (overall beta = sum of Type II error of each strain).
***PASS 2005 one-sided test on NI of mean under alternative hypotheses of GMT ratio = 1.0, Type I error = 2.5%.
****PASS 2005 one-sided test on NI of proportion under alternative hypotheses of SCR difference = 0%, Type I error = 2.5%.

If the primary objective was met, the following secondary objective would be tested to provide supportive evidence:

- CBER's SCR and SPR criteria would be checked for the FLU Q-QIV group for each of the four strains, approximately 28 days after completion of dosing (approximately Day 28 and Day 56 for vaccine-primed and -unprimed subjects, respectively).

CBER criteria to meet this objective:

- *lower limit of the two-sided 95% CI for SCR should be ≥ 40% for each strain.*
- *lower limit of the two-sided 95% CI for SPR should be ≥ 70% for each strain.*

The following table presents the statistical power needed to meet CBER criteria, with different reference values for SPR, assuming 1020 evaluable subjects in the Q-QIV vaccine group.

Table 17 Statistical power needed to meet CBER criteria of SCR and SPR for FLU Q-QIV

Endpoint	Criteria	Assumptions	N1=N2 (evaluable)	Power for 1 strain	Power for 4 strains
SCR	LL of 95% CI for SCR ≥ 40%	66.4%*	1020	>0.9999	>0.9999
SPR	LL of 95% CI for SPR ≥ 70%	**70.6%***	**1020**	**0.0612**	**0**
		72%	1020	0.2873	0
		74%	1020	0.8104	0.2416
		76%	1020	0.9911	0.9644
		78%	1020	>0.9999	>0.9999

*Based on results from FLU Q-QIV-021 (Q-QIV group), type I error = 2.5%.
Using Bonferonni adjustment on Type II error (overall beta = sum of Type II error of each strain).
PASS 2005 one-sided test on proportions Type I error = 2.5%.

The power calculations were based on the most conservative reference values from study FLU Q-QIV-021, 28 days after the last vaccination, which had SCR values ranging from 66.4%-86.0%, and SPR values of 87.4%, 82.5%, 94.4%, and 70.6% for A/H1N1, A/H3N2, B Yamagata and B Victoria, respectively. However, for the SPR with this reference (70.6%, observed for the B Victoria lineage) the power is very low, being 6% for a single strain. Hence, varying powers are presented in Table 17 for the SPR values, ranging from 70.6% to 78%. The low SPR values for B Victoria could be due to the fact that the B Victoria lineage circulated at a relatively low level in recent seasons [CDC, 2014]. For this study, the power to meet the CBER criteria for SPR would be expected to vary, depending on the trend for strain circulation in season 2014-2015.

Considering an attrition rate of 15%, it was determined that approximately 2400 subjects would have to be enrolled (~1200 subjects per group).

5.10.5. Study cohorts/data sets analyzed

5.10.5.1. Total vaccinated cohort

The Total vaccinated cohort (TVC) included all vaccinated subjects for whom data were available. Thus, for the analysis of safety, this included all subjects for whom safety data were available and for the analysis of immunogenicity, this included vaccinated subjects for whom immunogenicity endpoint measures were available. The Total vaccinated cohort analysis was performed per treatment actually administered.

5.10.5.2. According-to-protocol cohort for analysis of safety

The ATP cohort for analysis of safety included all vaccinated and eligible subjects

- who had received at least 1 dose of study vaccine/comparator according to their random assignment
- with sufficient data to perform an analysis of safety (1 dose with safety follow-up)
- for whom administration site of the study vaccine was known
- who had not received a vaccine not specified or forbidden in this protocol

- who did not meet any of the criteria for elimination from an ATP analysis

5.10.5.3. According-to-protocol cohort for analysis of immunogenicity

The ATP cohort for analysis of immunogenicity in terms of antibody response measured by the HI assay included all evaluable subjects (i.e., who meet all eligibility criteria, who complied with the procedures and intervals specified in the protocol, with no elimination criteria assigned during the study) for whom data concerning immunogenicity endpoint measures were available. This included subjects for whom assay results were available for antibodies against at least 1 study vaccine antigen component after vaccination and

- whose samples were collected within the interval allowed as defined in the protocol
- who did not meet any of the criteria for elimination from an ATP analysis
- who did not present a medical condition leading to exclusion from an ATP analysis

5.10.6. Derived and transformed data

- **Immunogenicity:**
  - The cut-off value was defined by the laboratory before the analysis and is described in Section 5.8.
  - A seronegative subject was a subject whose titer was below the cut-off value. A seropositive subject was a subject whose titer was greater than or equal to the cut-off value. For this study, HI titers of < 1:10 were considered below the cut-off.
  - The GMT calculations were performed by taking the anti-log of the mean of the log (base 10) transformed inverse titers (the number X would denote the inverse of a titer expressed as “1:X”). Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation.
  - The SCR was defined as the incidence rate of vaccinees who had either a pre-vaccination (Day 0) titer recorded as < 1:10 for HI and a post-vaccination titer ≥ 1:40 or a pre-vaccination titer ≥ 1:10 and at least a 4-fold increase in post-vaccination reciprocal titer.
  - The SPR was defined as the percentage of subjects who had a serum anti-HI antibody titer ≥ 1:40.
  - The MGI was defined as the geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer. MGIs were calculated on Day 28 following the complete vaccination regimen.
  - Handling of missing data: for a given subject and a given immunogenicity measurement, missing or non-evaluable measurements were not to be replaced. Therefore, analyses excluded subjects with missing or non-evaluable measurements.

- **Reactogenicity and Safety:**
  - Incidence rates of AEs were calculated as the number of subjects who experienced the event, divided by the number of subjects in the safety analysis cohort (the TVC or ATP cohort for analysis of safety).
  - Handling of missing data: For a given subject and the analysis of solicited AEs within 7 days post-vaccination (Days 0 through 6), missing or non-evaluable measurements were not to be replaced. Therefore, the analysis of the solicited AEs based on the TVC will included only vaccinated subjects and doses with documented safety data (i.e., symptom screen/sheet completed). Details of calculation of percentages of subjects with solicited or unsolicited AEs, as a percentage of doses or per subject, were to be contained in the Study Analysis Plan (SAP). In particular, for analysis of unsolicited AEs, such as SAEs or AEs by primary Medical Dictionary for Regulatory Activities (MedDRA) term, all vaccinated subjects were to be considered. Subjects who did not report the event were to be considered as subjects without the event.
  - For the analysis of unsolicited AEs/MAEs/SAEs/pIMDs/concomitant medications, all vaccinated subjects were to be considered and subjects who did not report an event were to be considered as subjects without an event.
  - For summaries reporting both solicited and unsolicited AEs, all vaccinated subjects were to be considered. Subjects who did not report the event were to be considered as subjects without the event.

All CIs were 95% CIs. The 95% CIs for GMT were obtained within each group separately. The 95% CI for the mean of lot-transformed titer was first obtained assuming that log-transformed titers were normally distributed with unknown variance. The 95% CI for the GMT was then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titer.

5.10.7. Analysis of demographics and other baseline characteristics

Demographic characteristics (age at first study vaccination , height and weight, gender, and race), were summarized by study group, age strata (all ages, 6-17, and 18-35 months of age) and priming status (primed and unprimed) using descriptive statistics:

- Frequency tables were generated for categorical variable such as center
- Mean, median and standard deviation were provided for continuous data such as age.
- Summary statistics for subjects' age classified by gender of the vaccinated subjects, as a whole, and per study group, were calculated
- The distribution of subjects enrolled among the study sites was tabulated as a whole and per group and classified subjects into disposition categories, including subjects who entered, completed, or withdrew from the study
- The proportion of subjects with prior immunologic experience with influenza vaccine(s) in the previous 3 influenza seasons were tabulated for each study group.

5.10.8. Analysis of immunogenicity

The primary analysis was based on the ATP cohort for analysis of immunogenicity. If, in any study group, the percentage of vaccinated subjects with serological results excluded from the ATP cohort for analysis of immunogenicity was 5% or more, a second analysis based on the Total vaccinated cohort was performed to complement the ATP analysis.

5.10.8.1. Within groups assessment

For the humoral immune response in terms of anti-HA antibodies against each of the 4 vaccine influenza strains, the following parameters (with 95% CIs) were calculated by each treatment group (FLU Q-QIV and *Fluzone Quadrivalent*) for all subjects, by age stratum (6 to 17 and 18 to 35 months of age) and by priming status (vaccine-primed and -unprimed):

- GMTs of anti-HA antibody titers at Day 0 and Day 28 following last vaccination
- SCRs at Day 28 following last vaccination.
- SPRs at Day 0 and Day 28 following last vaccination.
- MGI at Day 28 following last vaccination.

5.10.8.2. Between groups assessment

The GMT ratio and difference in SCR between groups were calculated to assess the immunogenic non-inferiority of FLU Q-QIV compared to *Fluzone Quadrivalent*:

The GMT ratio of *Fluzone Quadrivalent* over FLU Q-QIV and the two-sided 95% CI for each of the strains will be calculated.

The difference of SCR (*Fluzone Quadrivalent* minus FLU Q-QIV) and the two-sided 95% CI for each of the strains will be calculated.

The non-inferiority of FLU Q-QIV over Fluzone Quadrivalent was to be concluded if the upper limit of the two-sided 95% CI for the GMT ratio (Fluzone Quadrivalent/FLU Q-QIV) was ≤ 1.5 and the upper limit of the two-sided 95% CI on the SCR difference (Fluzone Quadrivalent minus FLU Q-QIV) was ≤ 10% for all strains in the overall population.

5.10.9. Analysis of safety

The primary analysis was performed on the Total vaccinated cohort. No complementary analysis was performed on the ATP cohort for safety (as specified in the protocol) since no additional value would be gained by performing the safety analysis on the ATP safety cohort (see Section 5.12.2, “Changes from planned analyses”).

5.10.9.1. Within groups assessment

For the analysis of vaccine safety, the following parameters (with 95% CI) were calculated by each treatment group for all subjects, by age stratum (6 to 17 and 18 to 35 months of age) and by priming status (primed, unprimed):

- The percentage of subjects with at least one solicited local AE, with at least one solicited general AE and with any AE during the 7-day follow-up period were tabulated with exact 95% CI after each vaccine dose and overall. The percentage of doses followed by at least one local AE (solicited only, see Section 5.12.2, "Changes from planned analyses"), by at least one general AE (solicited only, see Section 5.12.2, "Changes from planned analyses") and by any AE during the defined follow-up period were tabulated with exact 95% CI. The same calculations were performed for symptoms rated as Grade 3, related AEs and Grade 3 related AEs.
- The percentage of subjects reporting each individual solicited local (any, Grade 3, and medically attended) and general (any, Grade 3, related, Grade 3 related, and medically attended) AE during the 7-day solicited follow-up period were tabulated with exact 95% CI. All solicited local AEs were considered to be causally related. The percentage of doses followed by each individual solicited local and general AE during the 7-day solicited follow-up period were tabulated with exact 95% CI. The duration of the solicited symptoms were also be tabulated.
- The verbatim reports of unsolicited AEs that were reviewed by a physician and the signs and symptoms were coded according to the MedDRA. The percentage of subjects with at least one report of AE classified by MedDRA and reported up to 27 days after vaccination were tabulated with exact 95% CI. The same tabulation was performed for Grade 3 unsolicited AEs, for unsolicited AEs with a relationship to vaccination and Grade 3 unsolicited AEs with relationship to vaccination.
- MAEs, SAEs, and pIMDs were collected and summarized through the entire study period (180 days). In addition, SAEs and withdrawal due to AEs were described in detail.

5.10.9.2. Between groups assessment (exploratory analysis)

As an exploratory analysis, the relative risk of subjects with any fever (≥ 38°C) and Grade 3 or higher fever (> 39°C) during two days (48 hours) follow-up after any vaccine dose from the two vaccine groups was calculated for all subjects along with the 95% CI. However, these results (relative risks) should be interpreted with caution as no multiplicity adjustments were to be made.

5.10.10. Sequence of analyses

A single statistical analysis was performed on final and clean data at the end of the study (following the 6-month safety follow-up completion) when all the data were available.

5.10.11. Interim analysis

There was no interim analysis. All analyses were conducted on final data and, therefore, no statistical adjustment for multiple analyses was required.

5.11. Data quality assurance at study level

To ensure that the study procedures conformed across all investigator sites, the protocol, electronic case report form and safety reporting were reviewed with the investigator(s) and his/her/their personnel responsible for the conduct of the study by the Company representative(s) prior to study start. A multi-investigator meeting was held in Mexico and in the USA prior to study start.

Adherence to the protocol requirements and verification of data generation accuracy were achieved through monitoring visits to each investigator site. Computer checks and blinded review of subject tabulations were performed to ensure consistency of eCRF completion. All procedures were performed according to methodologies detailed in GlaxoSmithKline Biologicals Standard Operating Procedures (SOPs).

All protocol deviations collected during the study were reviewed by the GSK study team in order to identify important protocol deviations. Consistent with ICH E3 guidance, important deviations are defined as deviations that were likely to affect the interpretation of the results and/or led to exclusion of any subject data from an analysis. Important deviations include, but are not limited to, those related to study inclusion or exclusion criteria, adherence to the protocol, conduct of the study, subject management or subject assessment.

- Of note, there were two subjects (b) (6) and (b) (6) across two sites (210309 and 210664, respectively) in the USA who were entered and/or randomized in the Randomization System on Internet (SBIR) before the subject's parent(s)/ LAR(s) signed the Informed Consent Form (ICF). For subject (b) (6), the initial ICF date was correct, but because the site was unable to obtain a blood sample at the initial visit, the subject returned 9 days later to have blood obtained and the ICF was re-signed. Subject (b) (6) was randomized early (3 days prior to ICF signature) due to internet issues at the site and site staff wanted to confirm randomization via cell phone before the subjects's planned visit 3 days later. Other than the randomization, no study procedure was performed on these subjects before the Informed Consent was signed. The data from the impacted subjects have been used for study analyses.

Contract Research Organizations (CROs) were employed to perform the following functions according to an agreed contract. The CRO responsibilities were conducted according to GSK's SOPs or SOPs agreed between GSK and the CRO. The following contract organizations were involved in this study:

Clinical Study Monitoring and Site Management: Novella Inc. was used as a monitoring service in the USA. Monitoring was not outsourced in Mexico.

Sample management:

Quest Diagnostics (central laboratory) was contracted for interim sample storage (but no analysis).

Quest Diagnostics
26081 Avenue Hall, ≠ 150
Valencia, CA 91355, USA

Data Management activities:

Tata Consultancy Services
Millennium Business Park, Waterfall Plaza,
Building No.4/303, Sector 2, Mahape,
Navi Mumbai, 400 710, India

Independent Audit statement:

This study was subject to audit by GlaxoSmithKline's R&D Global Quality Compliance (GQC) - Clinical Development Quality Assurance (CDQA) department. Four US sites and one Mexico site were audited by CDQA as part of routine quality compliance assessments in accordance with appropriate regulatory requirements and guidelines.

5.12. Changes in the conduct of the study or planned analyses

5.12.1. Protocol amendments

There were 4 protocol amendments prior to study start.

In Protocol Amendment 1 (dated 09 July 2014), the original protocol dated 04 June 2014 was amended to modify the definitions of vaccine primed and unprimed subjects in order to harmonize with the ACIP recommendations for the 2014-15 influenza season and follow the updated recommended ACIP dosing schedule.

In Protocol Amendment 2 (dated 25 July 2014), an error was corrected in an exclusion criterion (the dose of prednisone in the criterion for persons who weigh ≥10 kg was erroneously listed as ≥20 mg/kg/day of prednisone, and was corrected to ≥20 mg/day of prednisone).

In Protocol Amendment 3 (dated 14 August 2014), the protocol was amended to comply with the local Mexican regulatory requirement to report all AEs during the entire study period. Therefore, for Mexican sites only, the collection period for unsolicited AEs was changed from only the Day 0-27 time period after each dose of vaccination, to the entire study period, i.e., from Day 0 to study conclusion. This change was only applicable for study sites in Mexico (although the amended document was also provided to study sites in the United States for informational purposes).

In addition, a general statement was added to Section 12, "Country Specific Requirements," to clarify that all countries and sites needed to follow applicable local regulations and guidelines during the study.

In Protocol Amendment 4 (dated 24 September 2014), Table 15 (Dosage and administration of study vaccines) was amended to correct an error, inadvertently introduced at the publication stage in the previous Amendment 3, which incorrectly changed the recommended injection site for subjects below 12 months of age from the left anterolateral thigh site to the non-dominant deltoid muscle site (the recommended site, left anterolateral thigh, was correctly indicated in Amendment 2).

Additionally, in response to study investigators' feedback, text was added to the first bullet in Protocol Section 6.7.1 ("Recording of concomitant medications/products and concomitant vaccination") to clarify that all concomitant medications/products needed to be recorded starting 30 days prior to the first dose of study vaccine and for 28 days following each dose of study vaccine.

5.12.2. Other changes (Changes in planned analyses)

Analyses were performed as planned in the protocol except for the following changes from planned analyses, which were recorded in the Statistical Analysis Plan (SAP) and finalized 2 months prior to study completion:

- All safety and reactogenicity analyses were to be done only on the Total vaccinated Cohort and no complementary analysis was to be performed on the ATP safety cohort (as specified in the protocol) as no additional value would be added by performing the safety analysis on the ATP safety cohort.
- Adverse events tabulation for 7 days post vaccination will be performed only for solicited adverse events instead of both solicited and unsolicited AEs (as specified in the protocol) as per the feedback from CBER.

Additionally, a post-hoc, exploratory analysis of the anti-HA response of study subjects was conducted to assess the potential impact of vaccine stability on the immunogenic response (see Section 7.3 for details). The immunogenic response (expressed as HI GMT values by treatment group) in the ATP cohort for immunogenicity was examined by the month the subjects received their last dose of study vaccine.

6. STUDY POPULATION RESULTS

6.1. Study dates

The first subject was enrolled in the study on 01-October-2014 and the last study contact was on 23-June-2015. The data lock point (date of database freeze) occurred on 18-August 2015.

6.2. Subject disposition

The number of subjects vaccinated, completed, or withdrawn from the study (with reasons for withdrawal), is presented in Table 18.

Table 18 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal (Total vaccinated cohort)

	Q-QIV	F-QIV	Total
Number of subjects vaccinated	1207	1217	2424
Number of subjects completed	1132	1139	2271
Number of subjects withdrawn	75	*78	153
Reasons for withdrawal:			
Serious Adverse Event	0	0	0
Non-Serious Adverse Event	0	0	0
Protocol violation	1	2	3
Consent withdrawal (not due to an adverse event)	15	10	25
Migrated/moved from study area	1	3	4
Lost to follow-up (subjects with incomplete vaccination course)	11	16	27
Lost to follow-up (subjects with complete vaccination course)	43	45	88
Sponsor study termination	0	0	0
Others	4	1	5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come back for the last visit
* One subject is not reflected in the table, but is included in the total of 78 subjects withdrawn from the F-QIV group. This subject (b) (6) withdrew at Visit 2 for undisclosed reasons, but permanent discontinuation was not recorded in the eCRF for this subject; however, the withdrawal was confirmed by site staff and also that no visit/study contact was done for the subject after Visit 2..

The number of subjects enrolled in the study at each center is presented in Table 41.

The number of subjects, who were withdrawn from the study at a particular study visit or phone contact, and the reasons for the withdrawal, is presented in Table 42.

6.3. Important Protocol deviations at subject level

6.3.1. Protocol Deviations leading to elimination from ATP analyses

Table 19 presents the number of subjects excluded from ATP analysis (with reasons for exclusion) as a result of protocol deviations.

- Most of the subject exclusions (n=242) occurred due to missing essential serological data (elimination code 2100; Table 19).
- Two subjects (b) (6) and (b) (6) were excluded after being administered a vaccine dose whose integrity could not be confirmed following a power failure at the study site.
- Two subjects (b) (6) and (b) (6) were excluded after being administered a vaccine with an incorrect treatment number (compared to the randomized treatment number) and it was unclear whether dose 1 was the same as dose 2.

Table 19 Number of subjects enrolled in the study and number of subjects excluded from ATP analyses with reasons for exclusion

	Total			Q-QIV		F-QIV		NOGRP	
Title	**n**	**s**	**%**	**n**	**s**	**n**	**s**	**n**	**s**
Total cohort	2430			1209		1220		1	
Study vaccine dose not administrated but subject number allocated (code 1030)	6	6		2	2	3	3	1	1
Total vaccinated cohort	2424		100	1207		1217		0	
Administration of vaccine(s) forbidden in the protocol (code 1040)	16	16		9	9	7	7	0	0
Randomisation failure (code 1050)	3	3		2	2	1	1	0	0
Study vaccine dose not administered according to protocol (code 1070)	1	1		0	0	1	1	0	0
Vaccine temperature deviation (code 1080)	5	6		2	3	3	3	0	0
ATP cohort for safety	2399		99.0	1194		1205		0	
Protocol violation (inclusion/exclusion criteria) (code 2010)	1	1		0	0	1	1	0	0
Administration of any medication forbidden by the protocol (code 2040)	6	7		4	4	2	3	0	0
Underlying medical condition forbidden by the protocol (code 2050)	2	3		1	1	1	2	0	0
Non compliance with vaccination schedule (including wrong and unknown dates) (code 2080)	24	24		13	13	11	11	0	0
Non compliance with blood sampling schedule (including wrong and unknown dates (code 2090)	79	81		38	40	41	41	0	0
Essential serological data missing (code 2100)	242	256		122	127	120	129	0	0
Others (immuno) (code 2500)	4	65		3	34	1	31	0	0
ATP cohort for immunogenicity	2041		84.2	1013		1028		0	

NOGRP = No assigned group
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Note: Subjects may have more than one elimination code assigned
n = number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
s = number of subjects with the elimination code assigned
% = percentage of subjects in the considered ATP cohort relative to the Total vaccinated cohort

The deviations from specifications for age and intervals between study visits for primed and unprimed subjects are presented in Table 43 and Table 44, respectively.

6.3.2. Protocol Deviations not leading to elimination from ATP analyses

Protocol deviations not leading to elimination for ATP analyses were the following:

- *Temperature taken via a non-protocol approved route:* For 15 subjects at center # 210149 in the USA, temperature was recorded via the temporal route, which was not consistent with the protocol.
- *No blood sample taken at Visit 1:* No blood sample was collected at Visit 1, in violation of the protocol, for 21 subjects across 9 centers in the USA.
- *Failure to report safety events per protocol:* Two subjects (b) (6) and (b) (6) at center # 210671 in the USA each experienced an SAE (dehydration in both cases), but there was a failure by site staff to report the two SAEs in a timely manner, as required by the study protocol.
- *Subjects incorrectly randomized:* Four subjects at 3 US centers were incorrectly randomized (3 subjects should have been randomized as unprimed, but were

designated as primed in error and vice versa for the fourth subject). However, these errors were corrected via a SBIR database correction form (DBCF) prior to the second study visit and all 4 subjects were then correctly randomized based on their priming status and followed the correct study procedures per protocol.

6.4. Demographic characteristics and other baseline characteristics

6.4.1. Demographic characteristics

The summary of demographic characteristics for TVC and ATP cohort for immunogenicity is presented in Table 20 and Table 21, respectively.

Table 20 Summary of demographic characteristics (Total vaccinated cohort)

		Q-QIV N = 1207		F-QIV N = 1217		Total N = 2424	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	19.4	-	19.5	-	19.5	-
	SD	8.7	-	8.9	-	8.8	-
	Median	19.0	-	19.0	-	19.0	-
	Minimum	6	-	6	-	6	-
	Maximum	35	-	36*	-	36	-
Gender	Female	547	45.3	582	47.8	1129	46.6
	Male	660	54.7	635	52.2	1295	53.4
Ethnicity	American Hispanic or Latino	305	25.3	302	24.8	607	25.0
	Not American Hispanic or Latino	902	74.7	915	75.2	1817	75.0
Geographic Ancestry	African Heritage / African American	190	15.7	187	15.4	377	15.6
	American Indian or Alaskan Native	29	2.4	24	2.0	53	2.2
	Asian - Central/South Asian Heritage	4	0.3	9	0.7	13	0.5
	Asian - East Asian Heritage	3	0.2	5	0.4	8	0.3
	Asian - Japanese Heritage	1	0.1	2	0.2	3	0.1
	Asian - South East Asian Heritage	18	1.5	23	1.9	41	1.7
	Native Hawaiian or Other Pacific Islander	4	0.3	10	0.8	14	0.6
	White - Arabic / North African Heritage	5	0.4	4	0.3	9	0.4
	White - Caucasian / European Heritage	770	63.8	781	64.2	1551	64.0
	Other	183	15.2	172	14.1	355	14.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation
*Pid (b) (6) is 36 months of age and was included in the subgroup 18-35M

Table 21 Summary of demographic characteristics (ATP cohort for immunogenicity)

		Q-QIV N = 1013		F-QIV N = 1028		Total N = 2041	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	19.7	-	19.9	-	19.8	-
	SD	8.7	-	8.9	-	8.8	-
	Median	20.0	-	20.0	-	20.0	-
	Minimum	6	-	6	-	6	-
	Maximum	35	-	35	-	35	-
Gender	Female	462	45.6	496	48.2	958	46.9
	Male	551	54.4	532	51.8	1083	53.1
Ethnicity	American Hispanic or Latino	249	24.6	262	25.5	511	25.0
	Not American Hispanic or Latino	764	75.4	766	74.5	1530	75.0
Geographic Ancestry	African Heritage / African American	143	14.1	140	13.6	283	13.9
	American Indian or Alaskan Native	23	2.3	18	1.8	41	2.0
	Asian - Central/South Asian Heritage	4	0.4	8	0.8	12	0.6
	Asian - East Asian Heritage	2	0.2	4	0.4	6	0.3
	Asian - Japanese Heritage	1	0.1	2	0.2	3	0.1
	Asian - South East Asian Heritage	17	1.7	20	1.9	37	1.8
	Native Hawaiian or Other Pacific Islander	4	0.4	8	0.8	12	0.6
	White - Arabic / North African Heritage	5	0.5	4	0.4	9	0.4
	White - Caucasian / European Heritage	647	63.9	667	64.9	1314	64.4
	Other	167	16.5	157	15.3	324	15.9

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

The age (in months) at vaccination Dose 1 by gender for the TVC and ATP cohort for immunogenicity, summary of vital characteristics at pre-vaccination, history of influenza vaccination in the previous 3 seasons and study population for the TVC is presented from Table 45 to Table 49.

The summary of demographic characteristics by age strata for the TVC and ATP cohort for immunogenicity is presented in Table 50 and Table 51, respectively.

The summary by age strata of vital characteristics, study population for the TVC, and history of influenza vaccination in the previous 3 seasons is presented from Table 52 to Table 54.

The summary of demographic characteristics by priming status for the TVC and ATP cohort for immunogenicity is presented in Table 55 and Table 56, respectively.

The age (in months) at vaccination Dose 1 by gender and by priming status for the TVC and ATP cohort for immunogenicity, summary of vital characteristics at pre-vaccination, history of influenza vaccination in the previous 3 seasons and study population by priming status for the TVC is presented from Table 57 to Table 61.

6.4.2. Other baseline characteristics

In addition to the demographics parameters, other baseline information about the study subjects was also collected. This included baseline medical history to help assess the incidence of risk factors for complications from influenza infections.

Baseline medical history of subjects indicating the presence of at least one risk factor that could predispose a subject to complications of influenza infection was reported in 6.8% and 6.2% of all subjects in the Q-QIV and F-QIV groups respectively (Table 95). The most frequent risk factor was chronic pulmonary disorder, including asthma (4.5% and 5.2% of subjects in the Q-QIV and F-QIV groups, respectively).

7. IMMUNOGENICITY RESULTS

The analysis of immunogenicity was performed on the ATP cohort for immunogenicity (primary analysis). Since the percentage of subjects eliminated from the ATP cohort was more than 5%, a second (complementary) analysis was performed on the TVC.

7.1. According-to-protocol analysis

7.1.1. Primary immunogenicity objective

7.1.1.1. Non-inferiority of FLU Q-QIV vs *Fluzone Quadrivalent* based on CBER's GMT and SCR criteria

The non-inferiority of FLU Q-QIV (Q-QIV) compared to *Fluzone Quadrivalent* (F-QIV) would be demonstrated if the following CBER criteria were met: the upper limit (UL) of the two-sided 95% CI for the GMT ratio (F-QIV/Q-QIV) was ≤ 1.5 and the upper limit of the two-sided 95% CI for the SCR difference (F-QIV minus Q-QIV) was ≤ 10% for all four vaccine strains.

This confirmatory primary objective was achieved since the results of the immunogenicity analysis indicated that, 28 days after the last vaccination, the non-inferiority criteria were met for all four vaccine strains in children 6-35 months of age (Table 22 and Table 23).

The UL of the two-sided 95% CI for the GMT ratio (F-QIV/Q-QIV), adjusted for baseline titer, for each strain was (Table 22; criterion: UL of 2-sided 95% CI for GMT ratio ≤ 1.5):

- 0.95 for A/California/7/2009 (H1N1)
- 0.94 for A/Texas/50/2012 (H3N2)
- 0.71 for B/Massachusetts/2/2012 (Yamagata Lineage)

- 0.69 for B/Brisbane/60/2008 (Victoria Lineage)

The UL of the two-sided 95% CI for the SCR difference (F-QIV minus Q-QIV) for each strain was (Table 23; criterion: UL of 2-sided 95% CI for SCR difference ≤ 10%):

- -2.27% for A/California/7/2009 (H1N1)
- -2.80% for A/Texas/50/2012 (H3N2)
- -12.02% for B/Brisbane/60/2008 (Victoria Lineage)
- -8.21% for B/Massachusetts/2/2012 (Yamagata Lineage)

Table 22 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV/Q-QIV (ATP cohort for immunogenicity)

					Adjusted GMT ratio (F-QIV / Q-QIV)		
	F-QIV		Q-QIV			95% CI	
Antibody	**N**	**Adjusted GMT**	**N**	**Adjusted GMT**	**Value**	**LL**	**UL**
A/California/7/2009 (H1N1)	980	85.1	972	99.6	0.85	0.77	**0.95**
A/Texas/50/2012 (H3N2)	980	84.6	972	99.8	0.85	0.77	**0.94**
B/Massachusetts/2/2012 (Yamagata)	980	167.3	974	258.1	0.65	0.59	**0.71**
B/Brisbane/60/2008 (Victoria)	980	33.7	973	54.5	0.62	0.56	**0.69**

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Adjusted GMT = geometric mean antibody titer adjusted for baseline titer
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

Table 23 SCR Difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV minus Q-QIV (ATP cohort for immunogenicity)

							Difference in SCR (F-QIV minus Q-QIV)		
	F-QIV			Q-QIV				95% CI	
Antibody	**N**	**n**	**%**	**N**	**n**	**%**	**%**	**LL**	**UL**
A/California/7/2009 (H1N1)	980	660	67.3	972	716	73.7	-6.32	-10.34	**-2.27**
A/Texas/50/2012 (H3N2)	980	680	69.4	972	740	76.1	-6.74	-10.68	**-2.80**
B/Brisbane/60/2008 (Victoria)	980	475	48.5	973	631	64.9	-16.38	-20.68	**-12.02**
B/Massachusetts/2/2012 (Yamagata)	980	723	73.8	974	833	85.5	-11.75	-15.28	**-8.21**

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
SCR defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

7.1.2. Secondary immunogenicity objective

A secondary immunogenicity objective was to assess whether the HI response elicited by FLU Q-QIV in children 6-35 months of age 28 days after the last vaccination, met CBER's SCR and SPR immunogenicity acceptance criteria i.e., the lower limit (LL) of the two-sided 95% CI for SCR should be ≥40% and the lower limit of the two-sided 95% CI for SPR should be ≥70%for each strain.

The study results indicated that, with the exception of the SPR criterion for the B/Victoria strain, the FLU Q-QIV immunogenic response met the SCR and SPR criteria for all strains (Table 24 and Table 25).

The LL of the two-sided 95% CI for the SCR for each strain in Q-QIV was (Table 24; criterion: LL of 2-sided 95% CI for SCR ≥ 40%):

- 70.8% for A/California/7/2009 (H1N1)
- 73.3% for A/Texas/50/2012 (H3N2)
- 83.2% for B/Massachusetts/2/2012 (Yamagata Lineage)
- 61.8% for B/Brisbane/60/2008 (Victoria Lineage)

The LL of the two-sided 95% CI for the SPR for each strain in Q-QIV was (Table 25; criterion: LL of 2-sided 95% CI for SPR difference ≥ 70%):

- 77.8% for A/California/7/2009 (H1N1)
- 79.7% for A/Texas/50/2012 (H3N2)
- 95.8% for B/Massachusetts/2/2012 (Yamagata Lineage)
- 63.0% for B/Brisbane/60/2008 (Victoria Lineage)

Table 24 Seroconversion rate (SCR) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for Q-QIV and F-QIV (ATP cohort for immunogenicity)

			SCR			
					95% CI	
Antibody	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/California/7/2009 (H1N1)	Q-QIV	972	716	73.7	**70.8**	76.4
	F-QIV	980	660	67.3	**64.3**	70.3
A/Texas/50/2012 (H3N2)	Q-QIV	972	740	76.1	**73.3**	78.8
	F-QIV	980	680	69.4	**66.4**	72.3
B/Massachusetts/2/2012 (Yamagata)	Q-QIV	974	833	85.5	**83.2**	87.7
	F-QIV	980	723	73.8	**70.9**	76.5
B/Brisbane/60/2008 (Victoria)	Q-QIV	973	631	64.9	**61.8**	67.9
	F-QIV	980	475	48.5	**45.3**	51.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
SCR defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL after vaccination
For initially seropositive subjects antibody titer after vaccination ≥ 4 fold the pre-vaccination antibody titer
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 25 Seropositivity rates, seroprotection rates (SPR) and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose (ATP cohort for immunogenicity)

				Seropositivity rate (≥ 10 1/DIL)				Seroprotection rate (≥ 40 1/DIL)				GMT				
						95% CI				95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	PRE	972	347	35.7	32.7	38.8	191	19.7	17.2	22.3	11.0	10.2	12.0	<10.0	7241.0
		POST	1013	947	93.5	91.8	94.9	814	80.4	**77.8**	82.8	98.8	90.3	108.2	<10.0	2560.0
	F-QIV	PRE	980	363	37.0	34.0	40.2	190	19.4	17.0	22.0	11.1	10.2	12.0	<10.0	905.0
		POST	1028	935	91.0	89.0	92.6	775	75.4	**72.6**	78.0	84.4	76.9	92.6	<10.0	3620.0
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	PRE	972	322	33.1	30.2	36.2	135	13.9	11.8	16.2	9.2	8.6	9.8	<10.0	3620.0
		POST	1013	982	96.9	95.7	97.9	833	82.2	**79.7**	84.5	97.7	90.3	105.7	<10.0	7241.0
	F-QIV	PRE	980	315	32.1	29.2	35.2	140	14.3	12.2	16.6	9.6	8.9	10.3	<10.0	2560.0
		POST	1028	978	95.1	93.6	96.4	800	77.8	**75.2**	80.3	84.3	77.6	91.6	<10.0	5120.0
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	PRE	974	689	70.7	67.8	73.6	324	33.3	30.3	36.3	20.3	18.8	22.0	<10.0	2560.0
		POST	1013	1013	100	99.6	100	983	97.0	**95.8**	98.0	257.5	240.9	275.3	10.0	7241.0
	F-QIV	PRE	980	683	69.7	66.7	72.6	336	34.3	31.3	37.4	20.6	19.0	22.4	<10.0	1280.0
		POST	1028	1020	99.2	98.5	99.7	911	88.6	**86.5**	90.5	164.2	151.8	177.6	<10.0	7241.0
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	PRE	973	130	13.4	11.3	15.7	40	4.1	3.0	5.6	6.2	6.0	6.5	<10.0	640.0
		POST	1013	939	92.7	90.9	94.2	669	66.0	63.0	69.0	55.1	50.8	59.8	<10.0	5120.0
	F-QIV	PRE	980	124	12.7	10.6	14.9	46	4.7	3.5	6.2	6.3	6.0	6.6	<10.0	1280.0
		POST	1028	837	81.4	78.9	83.8	512	49.8	46.7	52.9	33.4	30.6	36.4	<10.0	7241.0

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Seroprotection = HI antibody titer ≥ 40 1/DIL
GMT = geometric mean antibody titer calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titer within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

7.1.3. Descriptive immunogenicity analysis

Descriptive data on additional immunogenicity parameters (seropositivity rate, GMT, and Mean Geometric Increase [MGI]) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose for the ATP cohort for immunogenicity are presented in Table 25 and Table 26.

Table 26 Mean geometric increase (MGI) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose (ATP cohort for immunogenicity)

							GMT ratio			
									95% CI	
Antibody	Group	N	Time point description	GMT	Time point description	GMT	Ratio order	Value	LL	UL
A/California/7/2009 (H1N1)	Q-QIV	972	POST	99.5	PRE	11.0	POST / PRE	9.02	8.36	9.73
	F-QIV	980	POST	85.2	PRE	11.1	POST / PRE	7.69	7.09	8.34
A/Texas/50/2012 (H3N2)	Q-QIV	972	POST	98.6	PRE	9.2	POST / PRE	10.72	9.95	11.55
	F-QIV	980	POST	85.6	PRE	9.6	POST / PRE	8.93	8.24	9.68
B/Massachusetts/2/2012 (Yamagata)	Q-QIV	974	POST	257.2	PRE	20.3	POST / PRE	12.66	11.72	13.68
	F-QIV	980	POST	167.9	PRE	20.6	POST / PRE	8.14	7.53	8.80
B/Brisbane/60/2008 (Victoria)	Q-QIV	973	POST	54.3	PRE	6.2	POST / PRE	8.69	8.08	9.35
	F-QIV	980	POST	33.8	PRE	6.3	POST / PRE	5.37	4.99	5.78

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
MGI = Geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Seropositivity rates, seroprotection rates (SPRs), GMTs, SCRs, and MGIs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by age strata and priming status for ATP cohort for immunogenicity are presented in Table 66 and Table 71, respectively.

The reverse cumulative distribution curves of Flu A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata) and B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity) are presented from Figure 1 to Figure 4.

7.2. Total vaccinated cohort analysis

Since the percentage of vaccinated subjects with serological results excluded from the ATP cohort for analysis of immunogenicity was more than 5% (15.8%, Refer to Table 19), a second analysis based on the TVC was performed to complement the ATP analysis.

The results in the TVC were comparable to the results in the ATP Immunogenicity cohort.

The immunogenicity tables for the TVC are presented in Table 72 to Table 75.

7.3. Exploratory analysis of potential impact of vaccine stability on study subjects' immune response

In order to assess the potential impact of potency loss for two B strains observed in representative vaccine lots (see Section 5.4.1), the anti-HA immune response of subjects (expressed as HI GMT values by treatment group) in the ATP cohort for immunogenicity was examined by the month the subjects received their last dose of study vaccine, i.e., Dose 1 for primed subjects and Dose 2 for unprimed subjects. If the potency loss indeed resulted in a reduced immune response, the GMT values would be expected to decrease over time in the Q-QIV group, but not in the *Fluzone Quadrivalent* (F-QIV) control group, which was not affected by the potency loss.

As shown in Table 76 to Table 81 and Figure 5 to Figure 28, the per-strain GMT values for the Q-QIV group had modest random variation over time, most likely attributable to population differences enrolled over time and the imprecise estimations afforded by small sub-sample sizes. However, there were no decreases over time observed in the Q-QIV group overall or in the primed-unprimed strata. Moreover, the random variation observed in the Q-QIV group was also observed in the *Fluzone Quadrivalent* control group.

Therefore, this exploratory analysis of the immunogenicity data provided no evidence for a decrease in the GMTs over a period of several months for the two B strains in the study population, indicating that even if the minimal loss of potency observed for the B strains in the representative lots affected the vaccine lot used in the FLU Q-QIV-022 study, its magnitude was too small to have reduced the vaccine's anti-HA immunogenicity in this age group.

7.4. Immunogenicity summary

- The confirmatory primary objective to demonstrate immunogenic non-inferiority of FLU Q-QIV compared to *Fluzone Quadrivalent* vaccine in children 6-35 months of age 28 days after the last vaccination, was met for all four vaccine strains since the immunogenic response elicited by FLU Q-QIV fulfilled CBER's immunogenicity criteria (in terms of adjusted GMT ratio and difference in SCRs) for non-inferiority to a comparator vaccine.

- The CBER criteria specify an UL of the 2-sided 95% CI for the adjusted GMT ratio of ≤1.5 (the range of adjusted GMT ratios for F-QIV/Q-QIV was 0.69 to 0.95 for the 4 strains), and an UL of the 2-sided 95% CI for the difference in SCRs of ≤10% (the range of difference in SCRs for F-QIV minus Q-QIV was -12.02% to -2.27% for the 4 strains).

- A secondary immunogenicity objective was to assess whether the HI response elicited by FLU Q-QIV in children 6-35 months of age 28 days after the last vaccination, met CBER's SCR and SPR criteria for acceptable immunogenicity. The study results indicated that, with the exception of the SPR for the B/Victoria strain, the FLU Q-QIV immunogenic response met the SCR and SPR criteria.

  - The CBER criteria specify a LL of the 2-sided 95% CI for the SCR of ≥ 40% (the range for Q-QIV was 61.8% to 83.2% for the 4 strains), and a LL of the 2-sided 95% CI for the SPR of ≥ 70% (the value for the B/Victoria strain was 63.0% and the range for the other 3 strains was 77.8% to 95.8%).

8. SAFETY RESULTS

The analysis of safety was performed on the TVC (primary analysis).

Information regarding the number and percentage of subjects who received study vaccine per number of doses received is detailed in Table 27. Compliance in returning symptom sheets is presented in Table 82.

Table 27 Number and percentage of subjects who received study vaccine dose(s) (Total vaccinated cohort)

	Q-QIV N = 1207		F-QIV N = 1217	
Total number of doses received	**n**	**%**	**n**	**%**
1	688	57.0	688	56.5
2	519	43.0	529	43.5
Any	1207	100	1217	100

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = number of subjects in each group included in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least one dose

8.1. Total vaccinated cohort analysis

8.1.1. Overall incidence of solicited adverse events

The overall incidences of solicited AEs are detailed in Table 28, Table 29 (grade 3 AEs), Table 30 (AEs with causal relationship to vaccination), Table 31 (grade 3 AEs with causal relationship to vaccination).

- During the 7-day post-vaccination period, at least one solicited AE was reported for 74.1% and 71.6% of subjects in the Q-QIV and F-QIV groups, respectively.

At least one grade 3 solicited AE was reported for 11.0% and 8.1% of subjects in the Q-QIV and F-QIV groups, respectively. At least one solicited AE related to vaccination was reported for 68.2% and 65.7% of subjects in the Q-QIV and F-QIV groups, respectively. At least one grade 3 solicited AE related to vaccination was reported for 9.4% and 6.9% of subjects in the Q-QIV and F-QIV groups, respectively.

Table 28 Incidence and nature of solicited AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	1155	807	69.9	67.1	72.5	1155	707	61.2	58.3	64.0	1151	467	40.6	37.7	43.5
	F-QIV	1148	784	68.3	65.5	71.0	1148	698	60.8	57.9	63.6	1146	435	38.0	35.1	40.8
Dose 2	Q-QIV	490	294	60.0	55.5	64.4	490	265	54.1	49.6	58.6	490	139	28.4	24.4	32.6
	F-QIV	495	298	60.2	55.7	64.5	495	276	55.8	51.3	60.2	493	147	29.8	25.8	34.1
Overall/dose	Q-QIV	1645	1101	66.9	64.6	69.2	1645	972	59.1	56.7	61.5	1641	606	36.9	34.6	39.3
	F-QIV	1643	1082	65.9	63.5	68.1	1643	974	59.3	56.9	61.7	1639	582	35.5	33.2	37.9
Overall/subject	Q-QIV	1159	859	74.1	71.5	76.6	1159	768	66.3	63.5	69.0	1156	513	44.4	41.5	47.3
	F-QIV	1152	825	71.6	68.9	74.2	1152	749	65.0	62.2	67.8	1151	468	40.7	37.8	43.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 29 Incidence and nature of solicited grade 3 AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	1155	99	8.6	7.0	10.3	1155	82	7.1	5.7	8.7	1151	28	2.4	1.6	3.5
	F-QIV	1148	78	6.8	5.4	8.4	1148	71	6.2	4.9	7.7	1146	16	1.4	0.8	2.3
Dose 2	Q-QIV	490	40	8.2	5.9	11.0	490	34	6.9	4.9	9.6	490	9	1.8	0.8	3.5
	F-QIV	495	24	4.8	3.1	7.1	495	22	4.4	2.8	6.7	493	3	0.6	0.1	1.8
Overall/dose	Q-QIV	1645	139	8.4	7.2	9.9	1645	116	7.1	5.9	8.4	1641	37	2.3	1.6	3.1
	F-QIV	1643	102	6.2	5.1	7.5	1643	93	5.7	4.6	6.9	1639	19	1.2	0.7	1.8
Overall/subject	Q-QIV	1159	128	11.0	9.3	13.0	1159	109	9.4	7.8	11.2	1156	34	2.9	2.0	4.1
	F-QIV	1152	93	8.1	6.6	9.8	1152	84	7.3	5.9	8.9	1151	19	1.7	1.0	2.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 30 Incidence and nature of solicited AEs with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	1155	740	64.1	61.2	66.8	1155	596	51.6	48.7	54.5	1151	467	40.6	37.7	43.5
	F-QIV	1148	716	62.4	59.5	65.2	1148	595	51.8	48.9	54.8	1146	435	38.0	35.1	40.8
Dose 2	Q-QIV	490	265	54.1	49.6	58.6	490	222	45.3	40.8	49.8	490	139	28.4	24.4	32.6
	F-QIV	495	260	52.5	48.0	57.0	495	220	44.4	40.0	48.9	493	147	29.8	25.8	34.1
Overall/dose	Q-QIV	1645	1005	61.1	58.7	63.5	1645	818	49.7	47.3	52.2	1641	606	36.9	34.6	39.3
	F-QIV	1643	976	59.4	57.0	61.8	1643	815	49.6	47.2	52.1	1639	582	35.5	33.2	37.9
Overall/subject	Q-QIV	1159	790	68.2	65.4	70.8	1159	654	56.4	53.5	59.3	1156	513	44.4	41.5	47.3
	F-QIV	1152	757	65.7	62.9	68.5	1152	644	55.9	53.0	58.8	1151	468	40.7	37.8	43.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 31 Incidence and nature of solicited grade 3 AEs with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	1155	86	7.4	6.0	9.1	1155	65	5.6	4.4	7.1	1151	28	2.4	1.6	3.5
	F-QIV	1148	70	6.1	4.8	7.6	1148	63	5.5	4.2	7.0	1146	16	1.4	0.8	2.3
Dose 2	Q-QIV	490	32	6.5	4.5	9.1	490	26	5.3	3.5	7.7	490	9	1.8	0.8	3.5
	F-QIV	495	14	2.8	1.6	4.7	495	12	2.4	1.3	4.2	493	3	0.6	0.1	1.8
Overall/dose	Q-QIV	1645	118	7.2	6.0	8.5	1645	91	5.5	4.5	6.7	1641	37	2.3	1.6	3.1
	F-QIV	1643	84	5.1	4.1	6.3	1643	75	4.6	3.6	5.7	1639	19	1.2	0.7	1.8
Overall/subject	Q-QIV	1159	109	9.4	7.8	11.2	1159	86	7.4	6.0	9.1	1156	34	2.9	2.0	4.1
	F-QIV	1152	79	6.9	5.5	8.5	1152	70	6.1	4.8	7.6	1151	19	1.7	1.0	2.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

8.1.2. Solicited local adverse events

The incidence of solicited local AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall for the TVC is presented in Table 32.

The duration of the solicited local and general AEs during the 7-day follow-up period for the TVC is presented in Table 34.

- Overall, injection site pain was the most frequently reported solicited local AE (44.0% and 40.1% of subjects in the Q-QIV and F-QIV groups, respectively). Grade 3 injection site pain was reported for 2.9% and 1.7% of subjects, respectively.
- After Dose 1, the incidence of injection site pain was 40.3% and 37.4% of subjects in the Q-QIV and F-QIV groups, respectively. After Dose 2, the incidence of injection site pain was 28.2% and 29.8% of subjects, respectively.
- Redness at injection site was reported for 1.4% of subjects in each of the Q-QIV and F-QIV groups. Swelling at injection site was reported for 1.0% and 0.4% of subjects in the Q-QIV and F-QIV group, respectively. There were no reports of grade 3 redness or swelling.
- The median duration of any solicited local adverse events was between 1.0-2.0 days (Table 34).

Table 32 Incidence of solicited local AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Q-QIV					F-QIV				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Pain	All	1151	464	40.3	37.5	43.2	1146	429	37.4	34.6	40.3
	Grade 2 or 3	1151	150	13.0	11.1	15.1	1146	127	11.1	9.3	13.0
	Grade 3	1151	28	2.4	1.6	3.5	1146	16	1.4	0.8	2.3
	Medical advice	1151	0	0.0	0.0	0.3	1146	3	0.3	0.1	0.8
Redness (mm)	All	1151	15	1.3	0.7	2.1	1146	15	1.3	0.7	2.1
	>50	1151	5	0.4	0.1	1.0	1146	4	0.3	0.1	0.9
	>100	1151	0	0.0	0.0	0.3	1146	0	0.0	0.0	0.3
	Medical advice	1151	0	0.0	0.0	0.3	1146	2	0.2	0.0	0.6
Swelling (mm)	All	1151	11	1.0	0.5	1.7	1146	5	0.4	0.1	1.0
	>50	1151	2	0.2	0.0	0.6	1146	0	0.0	0.0	0.3
	>100	1151	0	0.0	0.0	0.3	1146	0	0.0	0.0	0.3
	Medical advice	1151	0	0.0	0.0	0.3	1146	0	0.0	0.0	0.3
Dose 2											
Pain	All	490	138	28.2	24.2	32.4	493	147	29.8	25.8	34.1
	Grade 2 or 3	490	31	6.3	4.3	8.9	493	36	7.3	5.2	10.0
	Grade 3	490	9	1.8	0.8	3.5	493	3	0.6	0.1	1.8
	Medical advice	490	0	0.0	0.0	0.8	493	0	0.0	0.0	0.7
Redness (mm)	All	490	1	0.2	0.0	1.1	493	2	0.4	0.0	1.5
	>50	490	0	0.0	0.0	0.8	493	0	0.0	0.0	0.7
	>100	490	0	0.0	0.0	0.8	493	0	0.0	0.0	0.7
	Medical advice	490	1	0.2	0.0	1.1	493	0	0.0	0.0	0.7
Swelling (mm)	All	490	0	0.0	0.0	0.8	493	0	0.0	0.0	0.7
	>50	490	0	0.0	0.0	0.8	493	0	0.0	0.0	0.7
	>100	490	0	0.0	0.0	0.8	493	0	0.0	0.0	0.7
	Medical advice	490	0	0.0	0.0	0.8	493	0	0.0	0.0	0.7
Overall/dose											
Pain	All	1641	602	36.7	34.3	39.1	1639	576	35.1	32.8	37.5
	Grade 2 or 3	1641	181	11.0	9.6	12.6	1639	163	9.9	8.5	11.5
	Grade 3	1641	37	2.3	1.6	3.1	1639	19	1.2	0.7	1.8
	Medical advice	1641	0	0.0	0.0	0.2	1639	3	0.2	0.0	0.5
Redness (mm)	All	1641	16	1.0	0.6	1.6	1639	17	1.0	0.6	1.7
	>50	1641	5	0.3	0.1	0.7	1639	4	0.2	0.1	0.6
	>100	1641	0	0.0	0.0	0.2	1639	0	0.0	0.0	0.2
	Medical advice	1641	1	0.1	0.0	0.3	1639	2	0.1	0.0	0.4
Swelling (mm)	All	1641	11	0.7	0.3	1.2	1639	5	0.3	0.1	0.7
	>50	1641	2	0.1	0.0	0.4	1639	0	0.0	0.0	0.2
	>100	1641	0	0.0	0.0	0.2	1639	0	0.0	0.0	0.2
	Medical advice	1641	0	0.0	0.0	0.2	1639	0	0.0	0.0	0.2
Overall/subject											
Pain	All	1156	509	44.0	41.1	46.9	1151	462	40.1	37.3	43.0
	Grade 2 or 3	1156	164	14.2	12.2	16.3	1151	150	13.0	11.1	15.1
	Grade 3	1156	34	2.9	2.0	4.1	1151	19	1.7	1.0	2.6
	Medical advice	1156	0	0.0	0.0	0.3	1151	3	0.3	0.1	0.8
Redness (mm)	All	1156	16	1.4	0.8	2.2	1151	16	1.4	0.8	2.2
	>50	1156	5	0.4	0.1	1.0	1151	4	0.3	0.1	0.9
	>100	1156	0	0.0	0.0	0.3	1151	0	0.0	0.0	0.3
	Medical advice	1156	1	0.1	0.0	0.5	1151	2	0.2	0.0	0.6

		Q-QIV					F-QIV				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Swelling (mm)	All	1156	11	1.0	0.5	1.7	1151	5	0.4	0.1	1.0
	>50	1156	2	0.2	0.0	0.6	1151	0	0.0	0.0	0.3
	>100	1156	0	0.0	0.0	0.3	1151	0	0.0	0.0	0.3
	Medical advice	1156	0	0.0	0.0	0.3	1151	0	0.0	0.0	0.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

8.1.3. Solicited general adverse events

The incidence of solicited general AEs reported during the 7-day (Day 0-6) post-vaccination period following each dose and overall for TVC is presented in Table 33.

- Overall, irritability/ fussiness was the most frequently reported solicited general AE (54.4% and 50.5% of subjects in the Q-QIV and F-QIV groups, respectively) followed by drowsiness (40.6% and 40.9% of subjects, in the Q-QIV and F-QIV groups, respectively) and loss of appetite (33.7% and 33.4% of subjects in the Q-QIV and F-QIV groups, respectively).
- Grade 3 irritability/fussiness was reported for 5.3% and 3.9% of subjects, respectively. Grade 3 drowsiness was reported for 3.1% and 3.0% of subjects, respectively. Grade 3 loss of appetite was reported for 2.2% and 1.6% of subjects, respectively.
- During the 7-day (Day 0-6) follow-up, fever (≥38°C) was reported for 7.9% and 7.5% of subjects in the Q-QIV and F-QIV groups, respectively. Grade 3 or higher fever (>39°C) was reported for 2.2% and 1.5% of subjects, respectively.
- Most of the solicited general AEs, reported during the 7 days post-vaccination period, were assessed by the investigator to be causally related to vaccination.
- The incidence of the solicited AEs was generally slightly lower after Dose 2 in comparison to Dose 1.
- The median duration of solicited general adverse events was between 1.0-2.0 days (Table 34).

Table 33 Incidence of solicited general AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Q-QIV					F-QIV				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1											
Drowsiness	All	1155	424	36.7	33.9	39.6	1148	424	36.9	34.1	39.8
	Grade 2 or 3	1155	132	11.4	9.7	13.4	1148	143	12.5	10.6	14.5
	Grade 3	1155	31	2.7	1.8	3.8	1148	30	2.6	1.8	3.7
	Related	1155	365	31.6	28.9	34.4	1148	381	33.2	30.5	36.0
	Grade 3 Related	1155	27	2.3	1.5	3.4	1148	28	2.4	1.6	3.5
	Medical advice	1155	12	1.0	0.5	1.8	1148	7	0.6	0.2	1.3
Fever/(Axillary) (°C)	All	1155	146	12.6	10.8	14.7	1148	147	12.8	10.9	14.9
	≥38	1155	65	5.6	4.4	7.1	1148	67	5.8	4.6	7.4
	>38.5	1155	33	2.9	2.0	4.0	1148	30	2.6	1.8	3.7
	>39.0	1155	16	1.4	0.8	2.2	1148	11	1.0	0.5	1.7
	>39.5	1155	11	1.0	0.5	1.7	1148	4	0.3	0.1	0.9
	>40.0	1155	2	0.2	0.0	0.6	1148	0	0.0	0.0	0.3
	Related	1155	41	3.5	2.6	4.8	1148	50	4.4	3.2	5.7
	≥38 Related	1155	41	3.5	2.6	4.8	1148	50	4.4	3.2	5.7
	>38.5 Related	1155	16	1.4	0.8	2.2	1148	19	1.7	1.0	2.6
	>39.0 Related	1155	8	0.7	0.3	1.4	1148	6	0.5	0.2	1.1
	>39.5 Related	1155	4	0.3	0.1	0.9	1148	3	0.3	0.1	0.8
	>40.0 Related	1155	0	0.0	0.0	0.3	1148	0	0.0	0.0	0.3
	Medical advice	1155	17	1.5	0.9	2.3	1148	10	0.9	0.4	1.6
Irritability / Fussiness	All	1155	570	49.4	46.4	52.3	1148	527	45.9	43.0	48.8
	Grade 2 or 3	1155	224	19.4	17.2	21.8	1148	192	16.7	14.6	19.0
	Grade 3	1155	44	3.8	2.8	5.1	1148	34	3.0	2.1	4.1
	Related	1155	499	43.2	40.3	46.1	1148	473	41.2	38.3	44.1
	Grade 3 Related	1155	37	3.2	2.3	4.4	1148	33	2.9	2.0	4.0
	Medical advice	1155	17	1.5	0.9	2.3	1148	12	1.0	0.5	1.8
Loss Of Appetite	All	1155	334	28.9	26.3	31.6	1148	328	28.6	26.0	31.3
	Grade 2 or 3	1155	83	7.2	5.8	8.8	1148	92	8.0	6.5	9.7
	Grade 3	1155	19	1.6	1.0	2.6	1148	15	1.3	0.7	2.1
	Related	1155	280	24.2	21.8	26.8	1148	290	25.3	22.8	27.9
	Grade 3 Related	1155	16	1.4	0.8	2.2	1148	14	1.2	0.7	2.0
	Medical advice	1155	14	1.2	0.7	2.0	1148	9	0.8	0.4	1.5
Dose 2											
Drowsiness	All	490	157	32.0	27.9	36.4	495	166	33.5	29.4	37.9
	Grade 2 or 3	490	43	8.8	6.4	11.6	495	53	10.7	8.1	13.8
	Grade 3	490	10	2.0	1.0	3.7	495	6	1.2	0.4	2.6
	Related	490	133	27.1	23.3	31.3	495	136	27.5	23.6	31.6
	Grade 3 Related	490	6	1.2	0.5	2.6	495	2	0.4	0.0	1.5
	Medical advice	490	5	1.0	0.3	2.4	495	6	1.2	0.4	2.6
Fever/(Axillary) (°C)	All	490	60	12.2	9.5	15.5	495	48	9.7	7.2	12.7
	≥38	490	31	6.3	4.3	8.9	495	22	4.4	2.8	6.7
	>38.5	490	17	3.5	2.0	5.5	495	11	2.2	1.1	3.9
	>39.0	490	9	1.8	0.8	3.5	495	6	1.2	0.4	2.6
	>39.5	490	4	0.8	0.2	2.1	495	1	0.2	0.0	1.1
	>40.0	490	3	0.6	0.1	1.8	495	0	0.0	0.0	0.7
	Related	490	22	4.5	2.8	6.7	495	14	2.8	1.6	4.7
	≥38 Related	490	20	4.1	2.5	6.2	495	13	2.6	1.4	4.4
	>38.5 Related	490	12	2.4	1.3	4.2	495	5	1.0	0.3	2.3
	>39.0 Related	490	6	1.2	0.5	2.6	495	2	0.4	0.0	1.5

		Q-QIV					F-QIV				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	>39.5 Related	490	2	0.4	0.0	1.5	495	0	0.0	0.0	0.7
	>40.0 Related	490	1	0.2	0.0	1.1	495	0	0.0	0.0	0.7
	Medical advice	490	9	1.8	0.8	3.5	495	7	1.4	0.6	2.9
Irritability / Fussiness	All	490	211	43.1	38.6	47.6	495	214	43.2	38.8	47.7
	Grade 2 or 3	490	75	15.3	12.2	18.8	495	71	14.3	11.4	17.7
	Grade 3	490	21	4.3	2.7	6.5	495	14	2.8	1.6	4.7
	Related	490	185	37.8	33.4	42.2	495	175	35.4	31.1	39.7
	Grade 3 Related	490	18	3.7	2.2	5.7	495	9	1.8	0.8	3.4
	Medical advice	490	7	1.4	0.6	2.9	495	11	2.2	1.1	3.9
Loss Of Appetite	All	490	110	22.4	18.8	26.4	495	116	23.4	19.8	27.4
	Grade 2 or 3	490	32	6.5	4.5	9.1	495	29	5.9	4.0	8.3
	Grade 3	490	8	1.6	0.7	3.2	495	5	1.0	0.3	2.3
	Related	490	91	18.6	15.2	22.3	495	87	17.6	14.3	21.2
	Grade 3 Related	490	4	0.8	0.2	2.1	495	2	0.4	0.0	1.5
	Medical advice	490	5	1.0	0.3	2.4	495	11	2.2	1.1	3.9
Overall/dose											
Drowsiness	All	1645	581	35.3	33.0	37.7	1643	590	35.9	33.6	38.3
	Grade 2 or 3	1645	175	10.6	9.2	12.2	1643	196	11.9	10.4	13.6
	Grade 3	1645	41	2.5	1.8	3.4	1643	36	2.2	1.5	3.0
	Related	1645	498	30.3	28.1	32.6	1643	517	31.5	29.2	33.8
	Grade 3 Related	1645	33	2.0	1.4	2.8	1643	30	1.8	1.2	2.6
	Medical advice	1645	17	1.0	0.6	1.6	1643	13	0.8	0.4	1.3
Fever/(Axillary) (°C)	All	1645	206	12.5	11.0	14.2	1643	195	11.9	10.3	13.5
	≥38	1645	96	5.8	4.8	7.1	1643	89	5.4	4.4	6.6
	>38.5	1645	50	3.0	2.3	4.0	1643	41	2.5	1.8	3.4
	>39.0	1645	25	1.5	1.0	2.2	1643	17	1.0	0.6	1.7
	>39.5	1645	15	0.9	0.5	1.5	1643	5	0.3	0.1	0.7
	>40.0	1645	5	0.3	0.1	0.7	1643	0	0.0	0.0	0.2
	Related	1645	63	3.8	3.0	4.9	1643	64	3.9	3.0	4.9
	≥38 Related	1645	61	3.7	2.8	4.7	1643	63	3.8	3.0	4.9
	>38.5 Related	1645	28	1.7	1.1	2.5	1643	24	1.5	0.9	2.2
	>39.0 Related	1645	14	0.9	0.5	1.4	1643	8	0.5	0.2	1.0
	>39.5 Related	1645	6	0.4	0.1	0.8	1643	3	0.2	0.0	0.5
	>40.0 Related	1645	1	0.1	0.0	0.3	1643	0	0.0	0.0	0.2
	Medical advice	1645	26	1.6	1.0	2.3	1643	17	1.0	0.6	1.7
Irritability / Fussiness	All	1645	781	47.5	45.0	49.9	1643	741	45.1	42.7	47.5
	Grade 2 or 3	1645	299	18.2	16.3	20.1	1643	263	16.0	14.3	17.9
	Grade 3	1645	65	4.0	3.1	5.0	1643	48	2.9	2.2	3.9
	Related	1645	684	41.6	39.2	44.0	1643	648	39.4	37.1	41.9
	Grade 3 Related	1645	55	3.3	2.5	4.3	1643	42	2.6	1.8	3.4
	Medical advice	1645	24	1.5	0.9	2.2	1643	23	1.4	0.9	2.1
Loss Of Appetite	All	1645	444	27.0	24.9	29.2	1643	444	27.0	24.9	29.2
	Grade 2 or 3	1645	115	7.0	5.8	8.3	1643	121	7.4	6.1	8.7
	Grade 3	1645	27	1.6	1.1	2.4	1643	20	1.2	0.7	1.9
	Related	1645	371	22.6	20.6	24.7	1643	377	22.9	20.9	25.1
	Grade 3 Related	1645	20	1.2	0.7	1.9	1643	16	1.0	0.6	1.6
	Medical advice	1645	19	1.2	0.7	1.8	1643	20	1.2	0.7	1.9
Overall/subject											
Drowsiness	All	1159	471	40.6	37.8	43.5	1152	471	40.9	38.0	43.8
	Grade 2 or 3	1159	160	13.8	11.9	15.9	1152	177	15.4	13.3	17.6
	Grade 3	1159	36	3.1	2.2	4.3	1152	34	3.0	2.1	4.1
	Related	1159	411	35.5	32.7	38.3	1152	425	36.9	34.1	39.8
	Grade 3 Related	1159	29	2.5	1.7	3.6	1152	29	2.5	1.7	3.6

		Q-QIV					F-QIV				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Medical advice	1159	15	1.3	0.7	2.1	1152	13	1.1	0.6	1.9
Fever/(Axillary) (°C)	All	1159	183	15.8	13.7	18.0	1152	178	15.5	13.4	17.7
	≥38	1159	91	7.9	6.4	9.6	1152	86	7.5	6.0	9.1
	>38.5	1159	48	4.1	3.1	5.5	1152	41	3.6	2.6	4.8
	>39.0	1159	25	2.2	1.4	3.2	1152	17	1.5	0.9	2.4
	>39.5	1159	15	1.3	0.7	2.1	1152	5	0.4	0.1	1.0
	>40.0	1159	5	0.4	0.1	1.0	1152	0	0.0	0.0	0.3
	Related	1159	62	5.3	4.1	6.8	1152	63	5.5	4.2	6.9
	≥38 Related	1159	60	5.2	4.0	6.6	1152	62	5.4	4.2	6.8
	>38.5 Related	1159	28	2.4	1.6	3.5	1152	24	2.1	1.3	3.1
	>39.0 Related	1159	14	1.2	0.7	2.0	1152	8	0.7	0.3	1.4
	>39.5 Related	1159	6	0.5	0.2	1.1	1152	3	0.3	0.1	0.8
	>40.0 Related	1159	1	0.1	0.0	0.5	1152	0	0.0	0.0	0.3
	Medical advice	1159	24	2.1	1.3	3.1	1152	17	1.5	0.9	2.4
Irritability / Fussiness	All	1159	630	54.4	51.4	57.3	1152	582	50.5	47.6	53.4
	Grade 2 or 3	1159	265	22.9	20.5	25.4	1152	229	19.9	17.6	22.3
	Grade 3	1159	61	5.3	4.0	6.7	1152	45	3.9	2.9	5.2
	Related	1159	558	48.1	45.2	51.1	1152	525	45.6	42.7	48.5
	Grade 3 Related	1159	52	4.5	3.4	5.8	1152	39	3.4	2.4	4.6
	Medical advice	1159	23	2.0	1.3	3.0	1152	22	1.9	1.2	2.9
Loss Of Appetite	All	1159	391	33.7	31.0	36.5	1152	385	33.4	30.7	36.2
	Grade 2 or 3	1159	109	9.4	7.8	11.2	1152	112	9.7	8.1	11.6
	Grade 3	1159	26	2.2	1.5	3.3	1152	19	1.6	1.0	2.6
	Related	1159	328	28.3	25.7	31.0	1152	337	29.3	26.6	32.0
	Grade 3 Related	1159	19	1.6	1.0	2.5	1152	16	1.4	0.8	2.2
	Medical advice	1159	17	1.5	0.9	2.3	1152	19	1.6	1.0	2.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 34 Number of days with solicited local and general AEs during the 7-day follow-up period (Total vaccinated cohort)

Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max
Drowsiness	Dose 1	Q-QIV	424	2.0	1.0	1.0	1.0	2.0	7.0
		F-QIV	424	2.0	1.0	1.0	1.5	2.0	7.0
	Dose 2	Q-QIV	157	2.0	1.0	1.0	2.0	2.0	7.0
		F-QIV	166	2.1	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	581	2.0	1.0	1.0	2.0	2.0	7.0
		F-QIV	590	2.0	1.0	1.0	2.0	2.0	7.0
Irritability / fussiness	Dose 1	Q-QIV	570	2.4	1.0	1.0	2.0	3.0	7.0
		F-QIV	527	2.5	1.0	1.0	2.0	3.0	7.0
	Dose 2	Q-QIV	211	2.5	1.0	1.0	2.0	3.0	7.0
		F-QIV	214	2.3	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	781	2.4	1.0	1.0	2.0	3.0	7.0
		F-QIV	741	2.4	1.0	1.0	2.0	3.0	7.0
Loss of appetite	Dose 1	Q-QIV	334	2.2	1.0	1.0	2.0	3.0	7.0
		F-QIV	328	2.3	1.0	1.0	2.0	3.0	7.0
	Dose 2	Q-QIV	110	2.5	1.0	1.0	2.0	3.0	7.0
		F-QIV	116	2.2	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	444	2.3	1.0	1.0	2.0	3.0	7.0
		F-QIV	444	2.3	1.0	1.0	2.0	3.0	7.0
Pain	Dose 1	Q-QIV	464	1.8	1.0	1.0	1.0	2.0	7.0
		F-QIV	429	1.8	1.0	1.0	2.0	2.0	6.0
	Dose 2	Q-QIV	138	1.7	1.0	1.0	1.0	2.0	6.0
		F-QIV	147	1.7	1.0	1.0	1.0	2.0	5.0
	Overall/dose	Q-QIV	602	1.8	1.0	1.0	1.0	2.0	7.0
		F-QIV	576	1.8	1.0	1.0	1.5	2.0	6.0
Redness	Dose 1	Q-QIV	15	2.0	1.0	1.0	2.0	3.0	4.0
		F-QIV	15	2.1	1.0	1.0	1.0	3.0	6.0
	Dose 2	Q-QIV	1	1.0	1.0	1.0	1.0	1.0	1.0
		F-QIV	2	1.5	1.0	1.0	1.5	2.0	2.0
	Overall/dose	Q-QIV	16	1.9	1.0	1.0	2.0	2.5	4.0
		F-QIV	17	2.0	1.0	1.0	1.0	2.0	6.0
Swelling	Dose 1	Q-QIV	11	2.4	1.0	1.0	2.0	3.0	5.0
		F-QIV	5	1.8	1.0	1.0	2.0	2.0	3.0
	Overall/dose	Q-QIV	11	2.4	1.0	1.0	2.0	3.0	5.0
		F-QIV	5	1.8	1.0	1.0	2.0	2.0	3.0
Fever	Dose 1	Q-QIV	146	2.0	1.0	1.0	1.0	2.0	7.0
		F-QIV	147	1.8	1.0	1.0	1.0	2.0	7.0
	Dose 2	Q-QIV	60	1.8	1.0	1.0	1.0	2.0	7.0
		F-QIV	48	2.1	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	206	1.9	1.0	1.0	1.0	2.0	7.0
		F-QIV	195	1.9	1.0	1.0	1.0	2.0	7.0

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = number of doses with the symptom
Q1 = 25th percentile
Q3 = 75th percentile

8.1.3.1. Relative risk of fever due to FLU Q-QIV compared to *Fluzone Quadrivalent* (F-QIV) during a 2-day and a 4-day follow-up period

The relative risk (i.e., ratio of Q-QIV to F-QIV) in percentage of subjects reporting fever during 2-day (Days 0-1) and the 4-day (Day 0-3) post-vaccination period following each dose and overall for the TVC is presented in Table 35 and Table 36, respectively.

The relative risk of any fever (≥38°C) for the subjects in the Q-QIV group compared to the subjects in the F-QIV group, during a 2-day (48 hours) follow-up period was 0.97 (overall/subject, 3.6% for Q-QIV vs. 3.7% for F-QIV) with a 95% CI of [0.62; 1.52] (p-value = 0.9777).

The relative risk of grade 3 or above fever (>39.0°C) for subjects in the Q-QIV group compared to the subjects in the F-QIV group, during a 2-day (48 hours) follow-up period was 1.49 (overall/subject, 0.8% for Q-QIV vs. 0.5% for F-QIV) with a 95% CI of [0.47; 5.09] (p-value = 0.6156).

Table 35 Relative risk between groups (Q-QIV/F-QIV) in percentage of subjects reporting a specified solicited general AE (Fever) during the 2-day (Days 0-1) post-vaccination period following each dose (Total vaccinated cohort)

								Relative Risk (Q-QIV over F-QIV)			
		Q-QIV			F-QIV				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Fever/(Axillary) (°C)	All	1155	63	5.5	1148	74	6.4	0.85	0.59	1.20	0.3736
	≥38	1155	30	2.6	1148	34	3.0	0.88	0.52	1.48	0.6899
	>38.5	1155	13	1.1	1148	15	1.3	0.86	0.38	1.94	0.8379
	>39.0	1155	6	0.5	1148	4	0.3	1.49	0.35	7.18	0.7614
	>39.5	1155	5	0.4	1148	1	0.1	4.97	0.56	235.05	0.2216
	>40.0	1155	0	0.0	1148	0	0.0	INF	0.00	INF	
	Related	1155	22	1.9	1148	33	2.9	0.66	0.37	1.17	0.1699
	≥38 Related	1155	22	1.9	1148	32	2.8	0.68	0.38	1.21	0.2120
	>38.5 Related	1155	8	0.7	1148	14	1.2	0.57	0.21	1.45	0.2798
	>39.0 Related	1155	3	0.3	1148	3	0.3	0.99	0.13	7.42	1.0000
	>39.5 Related	1155	2	0.2	1148	1	0.1	1.99	0.10	117.28	1.0000
	>40.0 Related	1155	0	0.0	1148	0	0.0	INF	0.00	INF	
	Medical advice	1155	4	0.3	1148	2	0.2	1.99	0.28	21.98	0.6932
Dose 2											
Fever/(Axillary) (°C)	All	490	21	4.3	495	22	4.4	0.96	0.50	1.84	1.0000
	≥38	490	12	2.4	495	10	2.0	1.21	0.48	3.13	0.8131
	>38.5	490	6	1.2	495	4	0.8	1.52	0.36	7.30	0.7414
	>39.0	490	3	0.6	495	2	0.4	1.52	0.17	18.14	0.9905
	>39.5	490	1	0.2	495	0	0.0	INF	0.03	INF	0.9949
	>40.0	490	0	0.0	495	0	0.0	INF	0.00	INF	
	Related	490	11	2.2	495	10	2.0	1.11	0.43	2.92	0.9812
	≥38 Related	490	9	1.8	495	9	1.8	1.01	0.36	2.87	1.0000
	>38.5 Related	490	4	0.8	495	3	0.6	1.35	0.23	9.20	0.9889
	>39.0 Related	490	3	0.6	495	1	0.2	3.03	0.24	159.10	0.6174
	>39.5 Related	490	1	0.2	495	0	0.0	INF	0.03	INF	0.9949
	>40.0 Related	490	0	0.0	495	0	0.0	INF	0.00	INF	
	Medical advice	490	4	0.8	495	1	0.2	4.04	0.40	199.00	0.3687

								Relative Risk (Q-QIV over F-QIV)			
		Q-QIV			F-QIV				95% CI		
Symptoms	**Type**	**N**	**n**	**%**	**N**	**n**	**%**	**RR**	**LL**	**UL**	**P-value**
Overall/dose											
Fever/(Axillary) (°C)	All	1645	84	5.1	1643	96	5.8	0.87	0.64	1.18	0.4077
	≥38	1645	42	2.6	1643	44	2.7	0.95	0.61	1.49	0.9097
	>38.5	1645	19	1.2	1643	19	1.2	1.00	0.50	1.99	1.0000
	>39.0	1645	9	0.5	1643	6	0.4	1.50	0.48	5.12	0.6089
	>39.5	1645	6	0.4	1643	1	0.1	5.99	0.73	275.66	0.1254
	>40.0	1645	0	0.0	1643	0	0.0	INF	0.00	INF	
	Related	1645	33	2.0	1643	43	2.6	0.77	0.47	1.23	0.2994
	≥38 Related	1645	31	1.9	1643	41	2.5	0.76	0.46	1.23	0.2864
	>38.5 Related	1645	12	0.7	1643	17	1.0	0.71	0.31	1.57	0.4563
	>39.0 Related	1645	6	0.4	1643	4	0.2	1.50	0.36	7.22	0.7554
	>39.5 Related	1645	3	0.2	1643	1	0.1	3.00	0.24	157.30	0.6259
	>40.0 Related	1645	0	0.0	1643	0	0.0	INF	0.00	INF	
	Medical advice	1645	8	0.5	1643	3	0.2	2.66	0.64	15.59	0.2273
Overall/subject											
Fever/(Axillary) (°C)	All	1159	82	7.1	1152	93	8.1	0.88	0.64	1.19	0.4261
	≥38	1159	42	3.6	1152	43	3.7	0.97	0.62	1.52	0.9777
	>38.5	1159	19	1.6	1152	19	1.6	0.99	0.50	1.98	1.0000
	>39.0	1159	9	0.8	1152	6	0.5	1.49	0.47	5.09	0.6156
	>39.5	1159	6	0.5	1152	1	0.1	5.96	0.72	274.32	0.1270
	>40.0	1159	0	0.0	1152	0	0.0	INF	0.00	INF	
	Related	1159	33	2.8	1152	42	3.6	0.78	0.48	1.26	0.3422
	≥38 Related	1159	31	2.7	1152	40	3.5	0.77	0.47	1.26	0.3296
	>38.5 Related	1159	12	1.0	1152	17	1.5	0.70	0.31	1.56	0.4484
	>39.0 Related	1159	6	0.5	1152	4	0.3	1.49	0.35	7.18	0.7614
	>39.5 Related	1159	3	0.3	1152	1	0.1	2.98	0.24	156.54	0.6296
	>40.0 Related	1159	0	0.0	1152	0	0.0	INF	0.00	INF	
	Medical advice	1159	8	0.7	1152	3	0.3	2.65	0.64	15.51	0.2305

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = 95% confidence interval for relative risk (Exact Conditional to total number of cases), LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Exact Test conditional to number of cases

Table 36 Relative risk between groups (Q-QIV/F-QIV) in percentage of subjects reporting a specified solicited general AE (Fever) during the 4 day (Days 0-3) post-vaccination period following each dose (Total vaccinated cohort)

								Relative Risk (Q-QIV over F-QIV)			
		Q-QIV			F-QIV				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Dose 1											
Fever/(Axillary) (°C)	All	1155	101	8.7	1148	104	9.1	0.97	0.73	1.28	0.8546
	≥38	1155	41	3.5	1148	47	4.1	0.87	0.56	1.35	0.5746
	>38.5	1155	19	1.6	1148	22	1.9	0.86	0.44	1.66	0.7404
	>39.0	1155	11	1.0	1148	7	0.6	1.56	0.55	4.75	0.4888
	>39.5	1155	7	0.6	1148	2	0.2	3.48	0.66	34.32	0.1827
	>40.0	1155	1	0.1	1148	0	0.0	INF	0.03	INF	1.0000
	Related	1155	32	2.8	1148	40	3.5	0.80	0.48	1.30	0.3950
	≥38 Related	1155	32	2.8	1148	39	3.4	0.82	0.49	1.34	0.4609
	>38.5 Related	1155	13	1.1	1148	16	1.4	0.81	0.36	1.79	0.6988
	>39.0 Related	1155	7	0.6	1148	5	0.4	1.39	0.38	5.56	0.7827
	>39.5 Related	1155	3	0.3	1148	2	0.2	1.49	0.17	17.85	1.0000
	>40.0 Related	1155	0	0.0	1148	0	0.0	INF	0.00	INF	
	Medical advice	1155	8	0.7	1148	6	0.5	1.33	0.40	4.63	0.7995
Dose 2											
Fever/(Axillary) (°C)	All	490	41	8.4	495	31	6.3	1.34	0.82	2.20	0.2696
	≥38	490	21	4.3	495	13	2.6	1.63	0.78	3.55	0.2182
	>38.5	490	14	2.9	495	6	1.2	2.36	0.85	7.48	0.1102
	>39.0	490	7	1.4	495	3	0.6	2.36	0.54	14.13	0.3355
	>39.5	490	2	0.4	495	0	0.0	INF	0.19	INF	0.4949
	>40.0	490	1	0.2	495	0	0.0	INF	0.03	INF	0.9949
	Related	490	17	3.5	495	11	2.2	1.56	0.69	3.69	0.3313
	≥38 Related	490	15	3.1	495	10	2.0	1.52	0.64	3.77	0.4097
	>38.5 Related	490	10	2.0	495	4	0.8	2.53	0.73	11.03	0.1734
	>39.0 Related	490	6	1.2	495	1	0.2	6.06	0.74	278.81	0.1217
	>39.5 Related	490	2	0.4	495	0	0.0	INF	0.19	INF	0.4949
	>40.0 Related	490	1	0.2	495	0	0.0	INF	0.03	INF	0.9949
	Medical advice	490	7	1.4	495	2	0.4	3.54	0.67	34.88	0.1747
Overall/dose											
Fever/(Axillary) (°C)	All	1645	142	8.6	1643	135	8.2	1.05	0.82	1.34	0.7261
	≥38	1645	62	3.8	1643	60	3.7	1.03	0.71	1.50	0.9333
	>38.5	1645	33	2.0	1643	28	1.7	1.18	0.69	2.02	0.6123
	>39.0	1645	18	1.1	1643	10	0.6	1.80	0.79	4.36	0.1860
	>39.5	1645	9	0.5	1643	2	0.1	4.49	0.93	42.75	0.0657
	>40.0	1645	2	0.1	1643	0	0.0	INF	0.19	INF	0.5006
	Related	1645	49	3.0	1643	51	3.1	0.96	0.63	1.45	0.9156
	≥38 Related	1645	47	2.9	1643	49	3.0	0.96	0.63	1.46	0.9140
	>38.5 Related	1645	23	1.4	1643	20	1.2	1.15	0.60	2.20	0.7638
	>39.0 Related	1645	13	0.8	1643	6	0.4	2.16	0.77	6.94	0.1679
	>39.5 Related	1645	5	0.3	1643	2	0.1	2.50	0.41	26.22	0.4541
	>40.0 Related	1645	1	0.1	1643	0	0.0	INF	0.03	INF	1.0000
	Medical advice	1645	15	0.9	1643	8	0.5	1.87	0.75	5.10	0.2111

								Relative Risk (Q-QIV over F-QIV)			
		Q-QIV			F-QIV				95% CI		
Symptoms	Type	N	n	%	N	n	%	RR	LL	UL	P-value
Overall/subject											
Fever/(Axillary) (°C)	All	1159	132	11.4	1152	128	11.1	1.02	0.80	1.32	0.8909
	≥38	1159	62	5.3	1152	59	5.1	1.04	0.72	1.52	0.8821
	>38.5	1159	33	2.8	1152	28	2.4	1.17	0.69	2.01	0.6256
	>39.0	1159	18	1.6	1152	10	0.9	1.79	0.78	4.34	0.1903
	>39.5	1159	9	0.8	1152	2	0.2	4.47	0.93	42.54	0.0669
	>40.0	1159	2	0.2	1152	0	0.0	INF	0.19	INF	0.5030
	Related	1159	49	4.2	1152	50	4.3	0.97	0.64	1.47	0.9759
	≥38 Related	1159	47	4.1	1152	48	4.2	0.97	0.64	1.49	0.9764
	>38.5 Related	1159	23	2.0	1152	20	1.7	1.14	0.60	2.19	0.7761
	>39.0 Related	1159	13	1.1	1152	6	0.5	2.15	0.76	6.91	0.1712
	>39.5 Related	1159	5	0.4	1152	2	0.2	2.48	0.41	26.10	0.4581
	>40.0 Related	1159	1	0.1	1152	0	0.0	INF	0.03	INF	1.0000
	Medical advice	1159	15	1.3	1152	8	0.7	1.86	0.74	5.08	0.2154

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For overall/dose:
N = number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95% CI = 95% confidence interval for relative risk (Exact Conditional to total number of cases), LL = Lower Limit, UL = Upper Limit
P-value = 2-sided Exact Test conditional to number of cases

8.1.4. Unsolicited adverse events

The occurrence of unsolicited AEs, grade 3 unsolicited AEs, AEs with causal relationship to vaccination, and grade 3 AEs with causal relationship to vaccination within the 28-day (Days 0-27) post-vaccination period for TVC, reported by the percentage of subjects and doses administered, are presented in Table 83 to Table 80.

- During the 28-day post-vaccination period, at least one unsolicited AE was reported for 45.5% and 44.1% of subjects in the Q-QIV and F-QIV groups, respectively. Upper respiratory tract infection (9.2% of subjects) was the most frequently reported AE in the Q-QIV group followed by cough (5.8% of subjects), diarrhoea and nasopharyngitis (both in 5.5% of subjects), and otitis media (5.1% of subjects). The F-QIV group followed a similar pattern, where upper respiratory tract infection (8.4% of subjects) was the most frequently reported AE followed by cough (6.3% of subjects), rhinorrhoea (6.2% of subjects), pyrexia (4.6% of subjects), diarrhoea and nasopharyngitis (both in 4.4% of subjects), and otitis media (4.0% of subjects).
- At least one grade 3 unsolicited AE was reported for 5.8% and 6.2% subjects in the Q-QIV and F-QIV groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 5.9% and 5.8 % of subjects, respectively. At least one grade 3 unsolicited AE with causal relationship to vaccination was reported for 0.6% and 0.7% subjects, respectively.

8.1.4.1. Medically attended events (MAEs)

The percentage of subjects reporting the occurrence of unsolicited AEs with MAEs during the entire study period for the TVC is presented in Table 37.

- At least one unsolicited AE with a medically attended visit during the entire study period was reported for 60.2% and 59.1% of subjects in the Q-QIV and F-QIV groups, respectively.
- Upper respiratory tract infection was the most frequently reported MAE in both groups (20.1% and 19.1% of subjects in the Q-QIV and F-QIV groups, respectively) followed by otitis media (16.1% and 18.2% of subjects in the Q-QIV and F-QIV groups, respectively).

Table 37 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit (MAEs) during the entire study period (Total vaccinated cohort)

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		727	60.2	57.4	63.0	719	59.1	56.3	61.9
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	2	0.2	0.0	0.6	7	0.6	0.2	1.2
	Iron deficiency anaemia (10022972)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Leukocytosis (10024378)	1	0.1	0.0	0.5	5	0.4	0.1	1.0
	Lymphadenitis (10025188)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Lymphadenopathy (10025197)	6	0.5	0.2	1.1	2	0.2	0.0	0.6
	Neutropenia (10029354)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
Congenital, familial and genetic disorders (10010331)	Cryptorchism (10011498)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Cytogenetic abnormality (10067477)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dermoid cyst (10012522)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Macrocephaly (10050183)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Phimosis (10034878)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Tibial torsion (10064515)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	10	0.8	0.4	1.5	11	0.9	0.5	1.6
	Deafness bilateral (10052556)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Deafness unilateral (10048812)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Ear discomfort (10052137)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Ear disorder (10014004)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Ear pain (10014020)	13	1.1	0.6	1.8	14	1.2	0.6	1.9
	Eustachian tube dysfunction (10015543)	6	0.5	0.2	1.1	1	0.1	0.0	0.5
	Eustachian tube obstruction (10015544)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Middle ear effusion (10062545)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Otorrhoea (10033101)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Tympanic membrane hyperaemia (10052154)	1	0.1	0.0	0.5	0	0.0	0.0	0.3

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
Eye disorders (10015919)	Astigmatism (10003569)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Blepharitis (10005148)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Chalazion (10008388)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Conjunctival haemorrhage (10010719)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Conjunctivitis allergic (10010744)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Dacryostenosis acquired (10053990)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Eye discharge (10015915)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Eyelid oedema (10015993)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Photophobia (10034960)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Strabismus (10042159)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Gastrointestinal disorders (10017947)	Abdominal hernia (10060954)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Abdominal pain (10000081)	4	0.3	0.1	0.8	2	0.2	0.0	0.6
	Abdominal pain upper (10000087)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Anal fissure (10002153)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Anal polyp (10002168)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Anal pruritus (10068172)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Anal skin tags (10002172)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Aphthous stomatitis (10002958)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Constipation (10010774)	7	0.6	0.2	1.2	10	0.8	0.4	1.5
	Dental caries (10012318)	4	0.3	0.1	0.8	1	0.1	0.0	0.5
	Diarrhoea (10012735)	39	3.2	2.3	4.4	40	3.3	2.4	4.4
	Epigastric discomfort (10053155)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Eructation (10015137)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Flatulence (10016766)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Food poisoning (10016952)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Gastrointestinal inflammation (10064147)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Gastrooesophageal reflux disease (10017885)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Haematochezia (10018836)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Intussusception (10022863)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Nausea (10028813)	6	0.5	0.2	1.1	1	0.1	0.0	0.5
	Oral disorder (10067621)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Post-tussive vomiting (10066220)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Stomatitis (10042128)	5	0.4	0.1	1.0	4	0.3	0.1	0.8
	Teething (10043183)	7	0.6	0.2	1.2	2	0.2	0.0	0.6
	Vomiting (10047700)	44	3.6	2.7	4.9	36	3.0	2.1	4.1
General disorders and administration site conditions (10018065)	Asthenia (10003549)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Crying (10011469)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Developmental delay (10012559)	4	0.3	0.1	0.8	5	0.4	0.1	1.0
	Fatigue (10016256)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Gait disturbance (10017577)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Influenza like illness (10022004)	3	0.2	0.1	0.7	3	0.2	0.1	0.7
	Local swelling (10024770)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pyrexia (10037660)	75	6.2	4.9	7.7	72	5.9	4.7	7.4
	Vaccination site rash (10069482)	0	0.0	0.0	0.3	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Vaccination site reaction (10059080)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Vessel puncture site haemorrhage (10054092)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Immune system disorders (10021428)	Allergy to animal (10001742)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Drug hypersensitivity (10013700)	5	0.4	0.1	1.0	5	0.4	0.1	1.0
	Food allergy (10016946)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Hypersensitivity (10020751)	4	0.3	0.1	0.8	4	0.3	0.1	0.8
	Immunodeficiency (10061598)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Multiple allergies (10028164)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Seasonal allergy (10048908)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Selective iga immunodeficiency (10039915)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Infections and infestations (10021881)	Abscess (10000269)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Abscess limb (10050473)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Acarodermatitis (10063409)	0	0.0	0.0	0.3	3	0.2	0.1	0.7
	Acute sinusitis (10001076)	10	0.8	0.4	1.5	14	1.2	0.6	1.9
	Acute tonsillitis (10001093)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Adenoiditis (10051223)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Atypical mycobacterial infection (10061663)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Body tinea (10005913)	3	0.2	0.1	0.7	3	0.2	0.1	0.7
	Bronchiolitis (10006448)	37	3.1	2.2	4.2	36	3.0	2.1	4.1
	Bronchitis (10006451)	10	0.8	0.4	1.5	25	2.1	1.3	3.0
	Candida infection (10074170)	4	0.3	0.1	0.8	7	0.6	0.2	1.2
	Candida nappy rash (10007135)	10	0.8	0.4	1.5	5	0.4	0.1	1.0
	Cellulitis (10007882)	6	0.5	0.2	1.1	8	0.7	0.3	1.3
	Clostridium difficile infection (10054236)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Conjunctivitis (10010741)	56	4.6	3.5	6.0	65	5.3	4.1	6.8
	Conjunctivitis bacterial (10061784)	5	0.4	0.1	1.0	2	0.2	0.0	0.6
	Conjunctivitis viral (10010755)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Coxsackie viral infection (10011261)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Croup infectious (10011416)	58	4.8	3.7	6.2	47	3.9	2.9	5.1
	Dacryocystitis (10011844)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Dermatophytosis (10012504)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Ear infection (10014011)	16	1.3	0.8	2.1	17	1.4	0.8	2.2
	Enterobiasis (10014881)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Exanthema subitum (10015586)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	External ear cellulitis (10015729)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Eye infection (10015929)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Folliculitis (10016936)	0	0.0	0.0	0.3	4	0.3	0.1	0.8
	Fungal infection (10017533)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Fungal skin infection (10017543)	5	0.4	0.1	1.0	1	0.1	0.0	0.5
	Furuncle (10017553)	3	0.2	0.1	0.7	0	0.0	0.0	0.3
	Gastroenteritis (10017888)	59	4.9	3.7	6.3	67	5.5	4.3	6.9
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Gastroenteritis viral (10017918)	19	1.6	1.0	2.4	5	0.4	0.1	1.0
	Genital candidiasis (10018143)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Groin abscess (10050269)	1	0.1	0.0	0.5	0	0.0	0.0	0.3

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Hand-foot-and-mouth disease (10019113)	10	0.8	0.4	1.5	13	1.1	0.6	1.8
	Herpangina (10019936)	2	0.2	0.0	0.6	4	0.3	0.1	0.8
	Hordeolum (10020377)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Impetigo (10021531)	7	0.6	0.2	1.2	7	0.6	0.2	1.2
	Infected bites (10021769)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Influenza (10022000)	23	1.9	1.2	2.8	28	2.3	1.5	3.3
	Laryngitis (10023874)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Lice infestation (10024424)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Localised infection (10024774)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Lower respiratory tract infection (10024968)	3	0.2	0.1	0.7	0	0.0	0.0	0.3
	Molluscum contagiosum (10027807)	1	0.1	0.0	0.5	4	0.3	0.1	0.8
	Myringitis bullous (10028659)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Nasopharyngitis (10028810)	51	4.2	3.2	5.5	46	3.8	2.8	5.0
	Neonatal candida infection (10028924)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Onychomycosis (10030338)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Oral candidiasis (10030963)	4	0.3	0.1	0.8	1	0.1	0.0	0.5
	Oropharyngeal candidiasis (10050346)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Otitis externa (10033072)	3	0.2	0.1	0.7	2	0.2	0.0	0.6
	Otitis media (10033078)	194	16.1	14.0	18.3	222	18.2	16.1	20.5
	Otitis media acute (10033079)	65	5.4	4.2	6.8	68	5.6	4.4	7.0
	Otitis media chronic (10033081)	2	0.2	0.0	0.6	6	0.5	0.2	1.1
	Paronychia (10034016)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Penile infection (10061912)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Periorbital cellulitis (10057182)	3	0.2	0.1	0.7	2	0.2	0.0	0.6
	Pharyngitis (10034835)	44	3.6	2.7	4.9	47	3.9	2.9	5.1
	Pharyngitis streptococcal (10034839)	21	1.7	1.1	2.6	23	1.9	1.2	2.8
	Pharyngotonsillitis (10049140)	3	0.2	0.1	0.7	6	0.5	0.2	1.1
	Pneumonia (10035664)	22	1.8	1.1	2.7	26	2.1	1.4	3.1
	Pneumonia bacterial (10060946)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Pneumonia mycoplasmal (10035724)	4	0.3	0.1	0.8	4	0.3	0.1	0.8
	Pneumonia viral (10035737)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Pseudomonas infection (10061471)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Rash pustular (10037888)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Respiratory syncytial virus bronchiolitis (10038718)	6	0.5	0.2	1.1	5	0.4	0.1	1.0
	Respiratory syncytial virus infection (10061603)	15	1.2	0.7	2.0	15	1.2	0.7	2.0
	Respiratory tract infection (10062352)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Respiratory tract infection viral (10062106)	3	0.2	0.1	0.7	2	0.2	0.0	0.6
	Rhinitis (10039083)	8	0.7	0.3	1.3	8	0.7	0.3	1.3
	Roseola (10039222)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Rotavirus infection (10067470)	1	0.1	0.0	0.5	0	0.0	0.0	0.3

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Scarlet fever (10039587)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Sinusitis (10040753)	31	2.6	1.8	3.6	43	3.5	2.6	4.7
	Sinusitis bacterial (10060841)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Skin candida (10054152)	2	0.2	0.0	0.6	4	0.3	0.1	0.8
	Skin infection (10040872)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Staphylococcal infection (10058080)	3	0.2	0.1	0.7	3	0.2	0.1	0.7
	Streptococcal infection (10061372)	4	0.3	0.1	0.8	5	0.4	0.1	1.0
	Subcutaneous abscess (10042343)	4	0.3	0.1	0.8	2	0.2	0.0	0.6
	Tinea capitis (10043866)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Tinea infection (10060889)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Tonsillitis (10044008)	10	0.8	0.4	1.5	11	0.9	0.5	1.6
	Tonsillitis streptococcal (10044013)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Tooth infection (10048762)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Tracheitis (10044302)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Tracheobronchitis viral (10061556)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Upper respiratory tract infection (10046306)	243	20.1	17.9	22.5	233	19.1	17.0	21.5
	Urinary tract infection (10046571)	8	0.7	0.3	1.3	11	0.9	0.5	1.6
	Vaginal infection (10046914)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Varicella (10046980)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Viral infection (10047461)	54	4.5	3.4	5.8	54	4.4	3.4	5.8
	Viral pharyngitis (10047473)	1	0.1	0.0	0.5	4	0.3	0.1	0.8
	Viral rash (10047476)	18	1.5	0.9	2.3	18	1.5	0.9	2.3
	Viral tonsillitis (10047480)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Viral upper respiratory tract infection (10047482)	18	1.5	0.9	2.3	22	1.8	1.1	2.7
	Vulvovaginitis (10047794)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Wound infection (10048038)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Animal bite (10002515)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Arthropod bite (10003399)	7	0.6	0.2	1.2	4	0.3	0.1	0.8
	Burns first degree (10006797)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Burns second degree (10006802)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Clavicle fracture (10009245)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Concussion (10010254)	3	0.2	0.1	0.7	0	0.0	0.0	0.3
	Contusion (10050584)	3	0.2	0.1	0.7	4	0.3	0.1	0.8
	Corneal abrasion (10010984)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Craniocerebral injury (10070976)	4	0.3	0.1	0.8	1	0.1	0.0	0.5
	Exposure to communicable disease (10049711)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Exposure to toxic agent (10053487)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Face injury (10050392)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Fall (10016173)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Foreign body (10070245)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Hand fracture (10019114)	0	0.0	0.0	0.3	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Head injury (10019196)	11	0.9	0.5	1.6	2	0.2	0.0	0.6
	Humerus fracture (10020462)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Injury (10022116)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Joint dislocation (10023204)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Joint injury (10060820)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Laceration (10023572)	16	1.3	0.8	2.1	8	0.7	0.3	1.3
	Ligament sprain (10024453)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Limb crushing injury (10064031)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Limb injury (10061225)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Lip injury (10055082)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Mouth injury (10049294)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Multiple injuries (10028224)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Procedural pain (10064882)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Radial head dislocation (10073749)	3	0.2	0.1	0.7	2	0.2	0.0	0.6
	Rib fracture (10039117)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Road traffic accident (10039203)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Skin abrasion (10064990)	4	0.3	0.1	0.8	1	0.1	0.0	0.5
	Splinter (10041662)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Thermal burn (10053615)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Tooth injury (10044043)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Ulna fracture (10045375)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Upper limb fracture (10061394)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Vaccination complication (10046861)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Wound (10052428)	2	0.2	0.0	0.6	3	0.2	0.1	0.7
	Wound complication (10053692)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Investigations (10022891)	Blood carbon monoxide (10005406)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Blood lead increased (10005642)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Body temperature increased (10005911)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Cardiac murmur (10007586)	4	0.3	0.1	0.8	1	0.1	0.0	0.5
	Heart rate increased (10019303)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Weight increased (10047899)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Metabolism and nutrition disorders (10027433)	Abnormal weight gain (10000188)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Breast milk substitute intolerance (10072187)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Decreased appetite (10061428)	3	0.2	0.1	0.7	6	0.5	0.2	1.1
	Dehydration (10012174)	9	0.7	0.3	1.4	6	0.5	0.2	1.1
	Failure to thrive (10016165)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Feeding disorder (10061148)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Feeding disorder of infancy or early childhood (10016318)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Hyponatraemia (10021036)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Lactose intolerance (10023681)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Obesity (10029883)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Overweight (10033307)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Pica (10035001)	0	0.0	0.0	0.3	2	0.2	0.0	0.6

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Back pain (10003988)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Blount's disease (10072255)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Flank pain (10016750)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Foot deformity (10061159)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Growing pains (10018745)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Growth retardation (10053759)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Head deformity (10061199)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Joint swelling (10023232)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Knee deformity (10062061)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Musculoskeletal pain (10028391)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Pain in extremity (10033425)	5	0.4	0.1	1.0	4	0.3	0.1	0.8
	Synovial cyst (10042858)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Tenosynovitis (10043261)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Torticollis (10044074)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	B precursor type acute leukaemia (10003890)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Haemangioma (10018814)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Melanocytic naevus (10027145)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Skin papilloma (10040907)	0	0.0	0.0	0.3	4	0.3	0.1	0.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	5	0.4	0.1	1.0	4	0.3	0.1	0.8
	Fine motor delay (10066088)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Gross motor delay (10069118)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Hemiplegia (10019468)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Language disorder (10074869)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Motor developmental delay (10070302)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Presyncope (10036653)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Seizure (10039906)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Sensory integrative dysfunction (10048871)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Speech disorder (10041466)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Speech disorder developmental (10041467)	7	0.6	0.2	1.2	4	0.3	0.1	0.8
	Tremor (10044565)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Pregnancy, puerperium and perinatal conditions (10036585)	Cephalhaematoma (10008014)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Psychiatric disorders (10037175)	Abnormal behaviour (10061422)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Autism spectrum disorder (10063844)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Eating disorder (10014062)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Head banging (10019191)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Insomnia (10022437)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Irritability (10022998)	6	0.5	0.2	1.1	2	0.2	0.0	0.6
	Libido disorder (10061221)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Middle insomnia (10027590)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Onychophagia (10057342)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Phonological disorder (10034925)	0	0.0	0.0	0.3	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Sleep disorder (10040984)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
Renal and urinary disorders (10038359)	Calculus urinary (10007027)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dysuria (10013990)	4	0.3	0.1	0.8	4	0.3	0.1	0.8
	Enuresis (10014928)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Pollakiuria (10036018)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Urinary incontinence (10046543)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Urinary tract disorder (10046566)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Urine odour abnormal (10057135)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	3	0.2	0.1	0.7	2	0.2	0.0	0.6
	Genital erythema (10054816)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Genital labial adhesions (10064162)	0	0.0	0.0	0.3	5	0.4	0.1	1.0
	Genital rash (10018175)	5	0.4	0.1	1.0	6	0.5	0.2	1.1
	Gynaecomastia (10018800)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Penile adhesion (10059636)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Pruritus genital (10037093)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Testicular retraction (10043348)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Vaginal discharge (10046901)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Asthma (10003553)	10	0.8	0.4	1.5	21	1.7	1.1	2.6
	Bronchial hyperreactivity (10066091)	12	1.0	0.5	1.7	12	1.0	0.5	1.7
	Bronchospasm (10006482)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Cough (10011224)	46	3.8	2.8	5.1	64	5.3	4.1	6.7
	Dyspnoea (10013968)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Epistaxis (10015090)	1	0.1	0.0	0.5	4	0.3	0.1	0.8
	Hypoxia (10021143)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Lower respiratory tract congestion (10075565)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Nasal congestion (10028735)	14	1.2	0.6	1.9	15	1.2	0.7	2.0
	Nasal discomfort (10052437)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Oropharyngeal pain (10068319)	4	0.3	0.1	0.8	0	0.0	0.0	0.3
	Pneumonitis (10035742)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pulmonary congestion (10037368)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Respiratory disorder (10038683)	7	0.6	0.2	1.2	13	1.1	0.6	1.8
	Respiratory distress (10038687)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Rhinitis allergic (10039085)	14	1.2	0.6	1.9	12	1.0	0.5	1.7
	Rhinorrhoea (10039101)	8	0.7	0.3	1.3	16	1.3	0.8	2.1
	Sinus congestion (10040742)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Sinus disorder (10062244)	0	0.0	0.0	0.3	3	0.2	0.1	0.7
	Sleep apnoea syndrome (10040979)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Sneezing (10041232)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Snoring (10041235)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Tonsillar hypertrophy (10044003)	0	0.0	0.0	0.3	3	0.2	0.1	0.7
	Upper-airway cough syndrome (10070488)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Wheezing (10047924)	20	1.7	1.0	2.5	12	1.0	0.5	1.7

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Blister (10005191)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Cafe au lait spots (10006926)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dermal cyst (10012426)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dermatitis (10012431)	8	0.7	0.3	1.3	2	0.2	0.0	0.6
	Dermatitis atopic (10012438)	7	0.6	0.2	1.2	16	1.3	0.8	2.1
	Dermatitis contact (10012442)	3	0.2	0.1	0.7	7	0.6	0.2	1.2
	Dermatitis diaper (10012444)	31	2.6	1.8	3.6	23	1.9	1.2	2.8
	Dry skin (10013786)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Ecchymosis (10014080)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Eczema (10014184)	4	0.3	0.1	0.8	17	1.4	0.8	2.2
	Eczema nummular (10014201)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Erythema (10015150)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Erythema multiforme (10015218)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Hand dermatitis (10058898)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Idiopathic urticaria (10021247)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Ingrowing nail (10022013)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Keratosis pilaris (10066295)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Miliaria (10027627)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Nail disorder (10028694)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Neurodermatitis (10029263)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Petechiae (10034754)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Prurigo (10037083)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Rash (10037844)	14	1.2	0.6	1.9	14	1.2	0.6	1.9
	Rash erythematous (10037855)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Rash generalised (10037858)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Rash macular (10037867)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Skin fissures (10040849)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Skin lesion (10040882)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Solar urticaria (10041307)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Urticaria (10046735)	17	1.4	0.8	2.2	10	0.8	0.4	1.5
	Urticaria papular (10046750)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Social circumstances (10041244)	Sexual abuse (10040461)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Surgical and medical procedures (10042613)	Adenoidectomy (10001230)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Umbilical hernia repair (10045462)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Vascular disorders (10047065)	Haematoma (10018852)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Kawasaki's disease (10023320)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pallor (10033546)	1	0.1	0.0	0.5	0	0.0	0.0	0.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

8.2. According-to-protocol cohort analysis

All safety and reactogenicity analyses were to be done only on the Total vaccinated Cohort and no complementary analysis was to be performed on the ATP safety cohort (as specified in the protocol) as no additional value would be added by performing the safety analysis on the ATP safety cohort.

8.3. Serious adverse events

The percentage of subjects reporting the occurrence of serious adverse events (SAEs), classified by MedDRA Primary System Organ Class and Preferred Term, during the entire study period for the TVC is presented in Table 38.

The SAE Listing Table is in Section 13.1 (Table 132) and the CIOMS reports for SAEs are in Section 13.2.

8.3.1. Fatal events

No fatal events were reported during the entire study period.

8.3.2. Non-fatal events

A total of 56 non-fatal SAEs were reported for 43 subjects during the entire study period. Of these, 29 SAEs were experienced by 22 subjects (1.8%) in the Q-QIV group and 28 SAEs were reported for 21 subjects (1.7%) in the F-QIV (*Fluzone Quadrivalent*) group.

None of the SAEs was assessed by the investigator to be causally related to vaccination. All SAEs in the Q-QIV group were reported as "resolved/recovered," with the exception of one case of Kawasaki's disease in subject (b) (6) and a case of croup in subject (b) (6) which were reported as "resolving/recovering" at the time of this report. All SAEs in the F-QIV group were also reported as resolved/recovered at the time of this report, with the exception of 4 SAEs in subjects (b) (6) (B precursor type acute leukaemia), (b) (6) (failure to thrive), and (b) (6) (developmental delay and hemiplegia).

Table 38 Percentage of subjects reporting the occurrence of serious adverse events (SAEs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire study period (Total vaccinated cohort)

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		22	1.8	1.1	2.7	21	1.7	1.1	2.6
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Intussusception (10022863)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
General disorders and administration site conditions (10018065)	Developmental delay (10012559)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Bronchiolitis (10006448)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Cellulitis (10007882)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Croup infectious (10011416)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Gastroenteritis (10017888)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Groin abscess (10050269)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Lower respiratory tract infection (10024968)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Otitis media acute (10033079)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Pharyngitis (10034835)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Pneumonia (10035664)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Respiratory syncytial virus bronchiolitis (10038718)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Respiratory syncytial virus infection (10061603)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Urinary tract infection (10046571)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Concussion (10010254)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Craniocerebral injury (10070976)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Multiple injuries (10028224)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	2	0.2	0.0	0.6	3	0.2	0.1	0.7
	Failure to thrive (10016165)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Hyponatraemia (10021036)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	B precursor type acute leukaemia (10003890)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Nervous system disorders (10029205)	Febrile convulsion (10016284)	5	0.4	0.1	1.0	4	0.3	0.1	0.8
	Hemiplegia (10019468)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Seizure (10039906)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Renal and urinary disorders (10038359)	Calculus urinary (10007027)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Hypoxia (10021143)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pneumonitis (10035742)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Social circumstances (10041244)	Sexual abuse (10040461)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Vascular disorders (10047065)	Kawasaki's disease (10023320)	1	0.1	0.0	0.5	0	0.0	0.0	0.3

Q-QIV = Flu Q-QIV

F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

8.4. Adverse events leading to premature discontinuation of study vaccine and/or study

No AEs or SAEs leading to premature discontinuation of study vaccine and/or study were reported in this study.

8.5. Other significant adverse events and AEs of specific interest

8.5.1. Potential immune-mediated diseases

The percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs), classified by MedDRA Primary System Organ Class and Preferred Term, during the entire study period for the TVC is presented in Table 39. A listing of the pIMDs is provided in Table 40.

There were two cases of pIMDs reported during the entire study period and both occurred after the first vaccination dose, but neither was assessed by the investigator as causally related to vaccination. One pIMD was in the Q-QIV group (subject (b) (6): Kawasaki's disease, also reported as an SAE; recovering/resolving at the time of this report) and the other in the F-QIV group (subject (b) (6) Erythema multiforme; reported recovered/resolved at the time of this report).

Table 39 Percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire study period (Total vaccinated cohort)

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		1	0.1	0.0	0.5	1	0.1	0.0	0.5
Skin and subcutaneous tissue disorders (10040785)	Erythema multiforme (10015218)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Vascular disorders (10047065)	Kawasaki's disease (10023320)	1	0.1	0.0	0.5	0	0.0	0.0	0.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 40 Listing of potential immune-mediated diseases (pIMDs) reported during the entire study period (Total vaccinated cohort)

Group	Patient ID	Country	Age at onset (M)	Gender	Race	Primary System Organ Class	Preferred term	Dose	Day of onset	Relation	SAE (Y/N)	Outcome	pIMD Source	Intensity
Q-QIV	(b) (6)	United States	17	Female	WHITE - CAUCASIAN / EUROPEAN HERITAGE	Vascular disorders	Kawasaki's disease	1	93	N	Y	Recovering/resolving	MedDRA and investigator	Not applicable
F-QIV	(b) (6)	United States	19	Male	WHITE - CAUCASIAN / EUROPEAN HERITAGE	Skin and subcutaneous tissue disorders	Erythema multiforme	1	119	N	N	Recovered/resolved	MedDRA and investigator	Mild

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent

8.5.2. Risks factors in the Risk Management Plan (RMP)

Certain AEs of specific interest were being considered for inclusion in the Risk Management Plan (RMP) for FLU Q-QIV. As such, these AEs were to be closely monitored as through the entire study period and reported as SAEs (for a list of these AEs, see Section 5.9.3.2).

There were 9 cases (4 subjects in the F-QIV group and 5 subjects in the Q-QIV group) of febrile seizure, an adverse event of specific interest (AESI) on the RMP monitoring list. All 9 events were reported as resolved/recovered and none were assessed by the investigator to be causally related to vaccination (Table 132).

8.6. Concomitant medications /vaccinations

The results regarding concomitant medications and vaccinations are detailed in Table 91 to Table 94.

During the entire study period:

- Concomitant medications were used by 60.3% and 60.6% of subjects in the Q-QIV and F-QIV groups, respectively.
- An antipyretic was taken by 39.5% and 38.9% of subjects, respectively. Antipyretics were taken prophylactically in anticipation of reaction to vaccination by 2.7% and 2.1% of subjects, respectively.
- An antibiotic was taken by 28.3% and 28.9% of subjects, respectively. No antibiotics were taken prophylactically.
- At least one concomitant vaccination was administered on the same day as the study vaccine to 23.4% and 20.5% of subjects in the Q-QIV and F-QIV groups, respectively. The most frequently administered concomitant vaccinations on the same day as study vaccination were Hepatitis A vaccine (received by 10.3% and 8.7% of subjects in the Q-QIV and F-QIV groups, respectively) followed by pneumococcal conjugate vaccine (received by 10.1% and 9.4% of subjects, respectively) and *Haemophilus influenzae* type b vaccine (received by 7.4% and 6.6% of subjects, respectively).

8.7. Safety summary

A descriptive summary of safety data is provided in this section. These data, together with the safety data from other studies will contribute to the safety evaluation of the product.

- *Overall incidence of solicited adverse events (AEs):* During the 7-day post-vaccination period, at least one solicited AE was reported for 74.1% and 71.6% of subjects in the Q-QIV and F-QIV groups, respectively. At least one grade 3 solicited AE was reported for 11.0% and 8.1% of subjects in the Q-QIV and F-QIV groups, respectively. At least one solicited AE related to vaccination was reported for 68.2%

and 65.7% of subjects in the Q-QIV and F-QIV groups, respectively. At least one grade 3 solicited AE related to vaccination was reported for 9.4% and 6.9% of subjects in the Q-QIV and F-QIV groups, respectively.

- *Solicited local AEs*: Overall, during the 7-day post-vaccination period, injection site pain was the most frequently reported solicited local AE (44.0% and 40.1% of subjects in the Q-QIV and F-QIV groups, respectively). Grade 3 injection site pain was reported for 2.9% and 1.7% of subjects, respectively.
- *Solicited general AEs*: Overall, during the 7-day post-vaccination period, irritability/ fussiness was the most frequently reported solicited general AE (54.4% and 50.5% of subjects in the Q-QIV and F-QIV groups, respectively) followed by drowsiness (40.6% and 40.9% of subjects, in the Q-QIV and F-QIV groups, respectively) and loss of appetite (33.7% and 33.4% of subjects in the Q-QIV and F-QIV groups, respectively).
- *Relative risk of fever:* The relative risk of any fever (≥38°C) for the subjects in the Q-QIV group compared to the subjects in the F-QIV group, during a 2-day (48 hours) follow-up period was 0.97 (overall/subject, 3.6% for Q-QIV vs. 3.7% for F-QIV) with a 95% CI of [0.62; 1.52] (p-value = 0.9777). The relative risk of grade 3 or above fever (>39.0°C) for subjects in the Q-QIV group compared to the subjects in the F-QIV group, during a 2-day (48 hours) follow-up period was 1.49 (overall/subject, 0.8% for Q-QIV vs. 0.5% for F-QIV) with a 95% CI of [0.47; 5.09] (p-value = 0.6156).
- *Unsolicited AEs*: During the 28-day post-vaccination period, at least one unsolicited AE was reported for 45.5% and 44.1% of subjects in the Q-QIV and F-QIV groups, respectively. Upper respiratory tract infection was the most frequently reported AE in both the Q-QIV and F-QIV groups (in 9.2% and 8.4% of subjects, respectively). At least one grade 3 unsolicited AE was reported for 5.8% and 6.2% subjects in the Q-QIV and F-QIV groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 5.9% and 5.8 % of subjects, respectively. At least one grade 3 unsolicited AE with causal relationship to vaccination was reported for 0.6% and 0.7% subjects, respectively.
- *MAEs*: At least one unsolicited AE with a medically attended visit during the entire study period was reported for 60.2% and 59.1% of subjects in the Q-QIV and F-QIV groups, respectively. Upper respiratory tract infection was the most frequently reported MAE in both groups (20.1% and 19.1% of subjects in the Q-QIV and F-QIV groups, respectively) followed by otitis media (16.1% and 18.2% of subjects in the Q-QIV and F-QIV groups, respectively).
- *pIMDs*: There were two cases of pIMDs reported during the entire study period and both occurred after the first vaccination dose, but neither was assessed by the investigator as causally related to vaccination. One pIMD was in the Q-QIV group (Kawasaki's disease, also reported as an SAE; recovering/resolving at the time of this report) and the other in the F-QIV group (Erythema multiforme; reported recovered/resolved at the time of this report).
- *SAEs*: A total of 56 non-fatal SAEs were reported for 43 subjects during the entire study period. Of these, 29 SAEs were experienced by 22 subjects (1.8%) in the Q-

QIV group and 27 SAEs were reported for 21 subjects (1.7%) in the F-QIV (*Fluzone Quadrivalent*) group. No SAE was deemed by the investigator to be causally related to vaccination. All SAEs in the Q-QIV group were reported as resolved/recovered (one SAE, Kawasaki's disease, was resolving/recovering) at the time of this report. All SAEs in the F-QIV group were also reported as resolved/recovered at the time of this report, with the exception of 4 SAEs (B precursor type acute leukaemia, failure to thrive, developmental delay and hemiplegia) reported in 3 subjects. No fatal events were reported during the entire study period.

- *Risk factors in the RMP:* Risk factors being considered for inclusion in the Q-QIV Risk Management Plan were to be reported as SAEs per study protocol. There were 9 cases of such a risk, febrile seizure (4 subjects in the F-QIV group and 5 subjects in the Q-QIV group). All 9 events were reported as resolved/recovered and none were assessed by the investigator as causally related to vaccination.

9. OVERALL CONCLUSIONS

- The confirmatory primary objective to demonstrate immunogenic non-inferiority of FLU Q-QIV (Q-QIV) compared to Fluzone Quadrivalent (F-QIV), in children 6-35 months of age 28 days after the last vaccination, was achieved since the immunogenic response elicited by FLU Q-QIV met CBER's non-inferiority immunogenicity criteria (in terms of adjusted GMT ratio and difference in SCRs) for all four vaccine strains.
- The confirmatory secondary objective to assess whether the HI response elicited by FLU Q-QIV in children 6-35 months of age 28 days after the last vaccination, met CBER's SCR and SPR criteria for acceptable immunogenicity. The study results indicated that, with the sole exception of the SPR criterion for the B/Victoria strain, the FLU Q-QIV immunogenic response met the SCR and SPR criteria.
- A full dose of Q-QIV (0.5mL) was more immunogenic with respect to the influenza B strains (post-hoc analysis) without incremental reactogenicity or safety effects in all subjects 6-17 months of age and in vaccine-unprimed subjects 6-35 months of age, as compared to the 0.25mL dose used for the F-QIV comparator.
- During the 28-day post-vaccination period, at least one unsolicited AE was reported for 45.5% and 44.1% of subjects in the Q-QIV and F-QIV groups, respectively. At least one grade 3 unsolicited AE was reported for 5.8% and 6.2% subjects in the Q-QIV and F-QIV groups, respectively. At least one unsolicited AE with causal relationship to vaccination was reported for 5.9% and 5.8 % of subjects, respectively. At least one grade 3 unsolicited AE with causal relationship to vaccination was reported for 0.6% and 0.7% subjects, respectively.
- At least one unsolicited AE with a medically attended visit during the entire study period was reported for 60.2% and 59.1% of subjects in the Q-QIV and F-QIV groups, respectively. In both groups, upper respiratory tract infection was the most frequently reported MAE followed by otitis media.

- There were two cases of pIMDs reported during the entire study period (one each in the Q-QIV and F-QIV groups), but neither was assessed by the investigator as causally related to vaccination.
- A total of 56 non-fatal SAEs were reported for 43 subjects during the entire study period (29 SAEs were experienced by 22 subjects [1.8%] in the Q-QIV group and 28 SAEs were reported for 21 subjects [1.7%] in the F-QIV group. There were 9 cases of febrile seizure (4 subjects in the F-QIV group and 5 subjects in the Q-QIV group) which were all reported as resolved/recovered. No SAE was deemed by the investigator to be causally related to vaccination and no fatal SAEs were reported.
- No other safety concerns were identified. The FLU Q-QIV and Fluzone Quadrivalent vaccines were generally well tolerated.

10. POST-TEXT TABLES AND FIGURES

10.1. Study population

Table 41 Number of subjects by center (Total vaccinated cohort)

	Q-QIV	F-QIV	Total	
Center	n	n	n	%
210113	43	44	87	3.6
210114	5	6	11	0.5
210116	42	42	84	3.5
210149	12	12	24	1.0
210151	9	9	18	0.7
210152	8	10	18	0.7
210153	15	16	31	1.3
210154	6	6	12	0.5
210155	51	51	102	4.2
210160	16	17	33	1.4
210162	16	16	32	1.3
210164	3	1	4	0.2
210280	13	13	26	1.1
210282	6	5	11	0.5
210283	8	9	17	0.7
210296	24	24	48	2.0
210297	30	32	62	2.6
210299	12	13	25	1.0
210300	7	7	14	0.6
210301	24	24	48	2.0
210302	3	1	4	0.2
210309	6	6	12	0.5
210310	20	18	38	1.6
210313	14	10	24	1.0
210314	14	16	30	1.2
210315	10	11	21	0.9
210316	27	28	55	2.3
210317	11	12	23	0.9
210318	5	3	8	0.3
210319	4	4	8	0.3
210320	34	36	70	2.9
210321	4	3	7	0.3
210323	5	4	9	0.4
210327	19	18	37	1.5
210328	4	5	9	0.4
210329	27	28	55	2.3
210639	19	17	36	1.5
210657	17	19	36	1.5
210658	12	12	24	1.0
210664	18	17	35	1.4
210665	20	20	40	1.7
210666	55	56	111	4.6
210667	24	23	47	1.9
210668	18	17	35	1.4
210669	10	12	22	0.9
210670	4	5	9	0.4

	Q-QIV	F-QIV	Total	
Center	**n**	**n**	**n**	**%**
210671	35	35	70	2.9
210672	20	18	38	1.6
210673	4	4	8	0.3
210675	18	21	39	1.6
210677	17	17	34	1.4
210814	19	20	39	1.6
210815	13	12	25	1.0
210816	30	33	63	2.6
210818	2	3	5	0.2
210821	13	12	25	1.0
210823	28	29	57	2.4
210826	1	2	3	0.1
210865	12	11	23	0.9
210867	22	20	42	1.7
211189	26	24	50	2.1
211558	60	60	120	5.0
212034	35	38	73	3.0
212773	19	21	40	1.7
212774	7	8	15	0.6
212890	15	12	27	1.1
212891	15	17	32	1.3
212947	42	42	84	3.5
All	1207	1217	2424	100

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
n = number of subjects included in each group or in total for a given center or for all centers
All = sum of all subjects in each group or in total (sum of all groups)
% = n/All x 100
Center = GSK Biologicals assigned center number

Table 42 Number of subjects at each visit and list of withdrawn subjects (Total vaccinated cohort)

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
Q-QIV	VISIT 1 DAY 0	1207		
			(b) (6)	Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Protocol violation
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				PI does not feel protocol requirements will be followed. The PI is Dr. Agnes Schultz.
				Lost to follow-up
				Consent withdrawal
				Migrated / moved from the study area
				Consent withdrawal
				Lost to follow-up
	VISIT 2 DAY 28	1176		
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Subject has been dropped from the study due to a language barrier between parent and research staff
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up*Consent withdrawal
				Lost to follow-up
				Parent withdrew consent due to not wanting to do any more blood draws.
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
	VISIT 3 DAY 56	518		
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Non compliance
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
	PHONE CONT D180	1132		
F-QIV	VISIT 1 DAY 0	1217		
				Consent withdrawal
				Migrated / moved from the study area
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Protocol violation
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Consent withdrawal
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Protocol violation
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up*Consent withdrawal
				Migrated / moved from the study area
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
	VISIT 2 DAY 28	117		
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Migrated / moved from the study area
				Lost to follow-up
				Lost to follow-up
	VISIT 3 DAY 56	520		
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Child was placed in foster care by family court.
	PHONE CONT D180	1139		
Total	VISIT 1 DAY 0	2424		
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Migrated / moved from the study area
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Protocol violation
				Consent withdrawal
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Consent withdrawal
				Consent withdrawal
				Protocol violation
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Consent withdrawal
				Consent withdrawal

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Protocol violation
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up*Consent withdrawal
				Migrated / moved from the study area
				PI does not feel protocol requirements will be followed. The PI is Dr. Agnes Schultz.
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Migrated / moved from the study area
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
	VISIT 2 DAY 28	2353		
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Subject has been dropped from the study due to a language barrier between parent and research staff
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Lost to follow-up*Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Parent withdrew consent due to not wanting to do any more blood draws.
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Consent withdrawal
				Consent withdrawal
				Consent withdrawal
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Migrated / moved from the study area
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
	VISIT 3 DAY 56	1038		
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
			(b) (6)	Non compliance
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Lost to follow-up
				Child was placed in foster care by family court.
				Lost to follow-up
				Lost to follow-up
	PHONE CONT D180	2271		

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = Number of subjects who are still in the study up to the visit
Withdrawn = Subject who did not return after the visit

Table 43 Deviations from specifications for age and intervals between study visits for primed subjects (Total vaccinated cohort)

		Age	Dose:1-PI(D28)
Group		**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days
Q-QIV	N	657	610
	n	0	14
	%	0.0	2.3
	range	12 to 35	24 to 56
F-QIV	N	657	615
	n	1	20
	%	0.2	3.3
	range	13 to 36	25 to 93

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Table 44 Deviations from specifications for age and intervals between study visits for unprimed subjects (Total vaccinated cohort)

		Age	Dose:1-Dose:2	Dose:2-PII(D56)
Group		**Protocol**	**Protocol**	**Protocol**
		from 6 to 35 months	from 25 to 42 days	from 25 to 42 days
Q-QIV	N	550	519	470
	n	0	15	26
	%	0.0	2.9	5.5
	range	6 to 35	25 to 93	19 to 85
F-QIV	N	560	529	477
	n	0	14	21
	%	0.0	2.6	4.4
	range	6 to 35	25 to 98	21 to 106

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Table 45 Age (in months) at vaccination Dose 1 by gender (Total vaccinated cohort)

Group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	F	547	547	19.5	8.5	6	35
	M	660	660	19.4	8.9	6	35
	Total	1207	1207	19.4	8.7	6	35
F-QIV*	F	582	582	19.8	8.8	6	36
	M	635	635	19.2	9	6	35
	Total	1217	1217	19.5	8.9	6	36
ALL	F	1129	1129	19.7	8.7	6	36
	M	1295	1295	19.3	8.9	6	35
	Total	2424	2424	19.5	8.8	6	36

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age
*Pid (b) (6) is 36 months of age and was included in the subgroup 18-35M

Table 46 Age (in months) at vaccination Dose 1 by gender (ATP cohort for immunogenicity)

Group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	F	462	462	19.7	8.5	6	35
	M	551	551	19.7	8.8	6	35
	Total	1013	1013	19.7	8.7	6	35
F-QIV	F	496	496	20.2	8.8	6	35
	M	532	532	19.6	9	6	35
	Total	1028	1028	19.9	8.9	6	35
ALL	F	958	958	20.0	8.6	6	35
	M	1083	1083	19.7	8.9	6	35
	Total	2041	2041	19.8	8.8	6	35

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 47 Summary of vital signs characteristics (Total vaccinated cohort)

		Q-QIV (N = 1207)	F-QIV (N = 1217)	Total (N = 2424)
Characteristics	Parameters	Value	Value	Value
Height (cm)	Mean	81.7	81.7	81.7
	SD	9.4	9.5	9.4
	Median	81.0	81.0	81.0
	Minimum	56.0	36.0	36.0
	Maximum	114.0	114.0	114.0
	Unknown	5	2	7
Weight (kg)	Mean	11.4	11.4	11.4
	SD	2.6	2.5	2.6
	Median	11.4	11.4	11.4
	Minimum	4.7	5.7	4.7
	Maximum	21.4	22.7	22.7
	Unknown	3	1	4

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 48 History of influenza vaccination in the previous 3 seasons (Total vaccinated cohort)

		Q-QIV N = 1207		F-QIV N = 1217		Total N = 2424	
Characteristics	**Parameters or Categories**	**n**	**%**	**n**	**%**	**n**	**%**
At least one season	Yes	674	55.8	677	55.6	1351	55.7
	No	533	44.2	540	44.4	1073	44.3
Season 2011-2012	Yes	8	0.7	13	1.1	21	0.9
Season 2012-2013	Yes	249	20.6	247	20.3	496	20.5
Season 2013-2014	Yes	624	51.7	619	50.9	1243	51.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = Total number of subjects
n= number of subjects with influenza vaccination during the specified season
% = n / Number of subjects with available results x 100

Table 49 Study population (Total vaccinated cohort)

Number of subjects	**Q-QIV**	**F-QIV**	**Total**
Planned, N	1200	1200	2400
Randomised, N (Total Vaccinated Cohort)	1207	1217	2424
Completed, n (%)	1132 (93.8)	1139 (93.6)	2271 (93.7)
Demographics	Q-QIV	F-QIV	Total
N (Total Vaccinated Cohort)	1207	1217	2424
Females:Males	547:660	582:635	1129:1295
Mean Age, months (SD)	19.4 (8.7)	19.5 (8.9)	19.5 (8.8)
Median Age, months (minimum, maximum)*	19 (6, 35)	19 (6, 36)	19 (6, 36)
White - Caucasian / European Heritage, n (%)	770 (63.8)	781 (64.2)	1551 (64.0)
African Heritage / African American, n (%)	190 (15.7)	187 (15.4)	377 (15.6)
Other, n (%)	183 (15.2)	172 (14.1)	355 (14.6)

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N = total number of subjects
n/% = number/percentage of subjects
SD = standard deviation
*Pid (b) (6) is 36 months of age and was included in the subgroup 18-35M

Table 50 Summary of demographic characteristics by age strata (Total vaccinated cohort)

		Q-QIV				F-QIV				Total			
		6-17M N = 500		18-35M N = 707		6-17M N = 502		18-35M N = 715		6-17M N = 1002		18-35M N = 1422	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	10.6	-	25.7	-	10.4	-	25.9	-	10.5	-	25.8	-
	SD	3.5	-	5.3	-	3.5	-	5.2	-	3.5	-	5.3	-
	Median	10.0	-	25.0	-	10.0	-	25.0	-	10.0	-	25.0	-
	Minimum	6	-	18	-	6	-	18	-	6	-	18	-
	Maximum	17	-	35	-	17	-	36*	-	17	-	36	-
Gender	Female	227	45.4	320	45.3	227	45.2	355	49.7	454	45.3	675	47.5
	Male	273	54.6	387	54.7	275	54.8	360	50.3	548	54.7	747	52.5
Ethnicity	American Hispanic or Latino	118	23.6	187	26.4	102	20.3	200	28.0	220	22.0	387	27.2
	Not American Hispanic or Latino	382	76.4	520	73.6	400	79.7	515	72.0	782	78.0	1035	72.8
Geographic Ancestry	African Heritage / African American	75	15.0	115	16.3	82	16.3	105	14.7	157	15.7	220	15.5
	American Indian or Alaskan Native	10	2.0	19	2.7	9	1.8	15	2.1	19	1.9	34	2.4
	Asian - Central/South Asian Heritage	2	0.4	2	0.3	3	0.6	6	0.8	5	0.5	8	0.6
	Asian - East Asian Heritage	1	0.2	2	0.3	2	0.4	3	0.4	3	0.3	5	0.4
	Asian - Japanese Heritage	0	0.0	1	0.1	0	0.0	2	0.3	0	0.0	3	0.2
	Asian - South East Asian Heritage	5	1.0	13	1.8	7	1.4	16	2.2	12	1.2	29	2.0
	Native Hawaiian or Other Pacific Islander	1	0.2	3	0.4	7	1.4	3	0.4	8	0.8	6	0.4
	White - Arabic / North African Heritage	3	0.6	2	0.3	1	0.2	3	0.4	4	0.4	5	0.4
	White - Caucasian / European Heritage	326	65.2	444	62.8	326	64.9	455	63.6	652	65.1	899	63.2
	Other	77	15.4	106	15.0	65	12.9	107	15.0	142	14.2	213	15.0

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation
*Pid (b) (6) was 36 months of age and was included in the subgroup 18-35M

Table 51 Summary of demographic characteristics by age strata (ATP cohort for immunogenicity)

		Q-QIV				F-QIV				Total			
		6-17M N = 400		18-35M N = 613		6-17M N = 401		18-35M N = 627		6-17M N = 801		18-35M N = 1240	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	10.6	-	25.6	-	10.4	-	26.0	-	10.5	-	25.8	-
	SD	3.5	-	5.3	-	3.5	-	5.2	-	3.5	-	5.3	-
	Median	11.0	-	25.0	-	10.0	-	26.0	-	10.0	-	25.0	-
	Minimum	6	-	18	-	6	-	18	-	6	-	18	-
	Maximum	17	-	35	-	17	-	35	-	17	-	35	-
Gender	Female	181	45.3	281	45.8	182	45.4	314	50.1	363	45.3	595	48.0
	Male	219	54.8	332	54.2	219	54.6	313	49.9	438	54.7	645	52.0
Ethnicity	American Hispanic or Latino	90	22.5	159	25.9	84	20.9	178	28.4	174	21.7	337	27.2
	Not American Hispanic or Latino	310	77.5	454	74.1	317	79.1	449	71.6	627	78.3	903	72.8
Geographic Ancestry	African Heritage / African American	50	12.5	93	15.2	55	13.7	85	13.6	105	13.1	178	14.4
	American Indian or Alaskan Native	8	2.0	15	2.4	5	1.2	13	2.1	13	1.6	28	2.3
	Asian - Central/South Asian Heritage	2	0.5	2	0.3	2	0.5	6	1.0	4	0.5	8	0.6
	Asian - East Asian Heritage	1	0.3	1	0.2	2	0.5	2	0.3	3	0.4	3	0.2
	Asian - Japanese Heritage	0	0.0	1	0.2	0	0.0	2	0.3	0	0.0	3	0.2
	Asian - South East Asian Heritage	5	1.3	12	2.0	7	1.7	13	2.1	12	1.5	25	2.0
	Native Hawaiian or Other Pacific Islander	1	0.3	3	0.5	5	1.2	3	0.5	6	0.7	6	0.5
	White - Arabic / North African Heritage	3	0.8	2	0.3	1	0.2	3	0.5	4	0.5	5	0.4
	White - Caucasian / European Heritage	264	66.0	383	62.5	263	65.6	404	64.4	527	65.8	787	63.5
	Other	66	16.5	101	16.5	61	15.2	96	15.3	127	15.9	197	15.9

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 52 Summary of vital signs characteristics by age strata (Total vaccinated cohort)

		Q-QIV		F-QIV		Total	
		6-17M N = 500	18-35M N = 707	6-17M N = 502	18-35M N = 715	6-17M N = 1002	18-35M N = 1422
Characteristics	Parameters	Value	Value	Value	Value	Value	Value
Height (cm)	Mean	73.3	87.7	73.0	87.9	73.1	87.8
	SD	5.5	6.5	5.7	6.2	5.6	6.4
	Median	74.0	89.0	74.0	89.0	74.0	89.0
	Minimum	58.0	56.0	36.0	61.0	36.0	56.0
	Maximum	94.0	114.0	99.0	114.0	99.0	114.0
	Unknown	1	4	0	2	1	6
Weight (kg)	Mean	9.3	12.9	9.3	12.9	9.3	12.9
	SD	1.6	2.0	1.6	2.0	1.6	2.0
	Median	9.2	12.8	9.2	12.8	9.2	12.8
	Minimum	4.7	6.4	5.7	5.7	4.7	5.7
	Maximum	15.2	21.4	14.2	22.7	15.2	22.7
	Unknown	1	2	0	1	1	3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 53 Study population by age strata (Total vaccinated cohort)

	Q-QIV		F-QIV		Total	
Number of subjects	**6-17M**	**18-35M**	**6-17M**	**18-35M**	**6-17M**	**18-35M**
Planned, N						
Randomised, N (Total Vaccinated Cohort)	500	707	502	715	1002	1422
Completed, n (%)	462 (92.4)	670 (94.8)	457 (91.0)	682 (95.4)	919 (91.7)	1352 (95.1)
Demographics	6-17M	18-35M	6-17M	18-35M	6-17M	18-35M
N (Total Vaccinated Cohort)	500	707	502	715	1002	1422
Females:Males	227:273	320:387	227:275	355:360	454:548	675:747
Mean Age, months (SD)	10.6 (3.5)	25.7 (5.3)	10.4 (3.5)	25.9 (5.2)	10.5 (3.5)	25.8 (5.3)
Median Age, months (minimum, maximum)*	10 (6, 17)	25 (18, 35)	10 (6, 17)	25 (18, 36)	10 (6, 17)	25 (18, 36)
White - Caucasian / European Heritage, n (%)	326 (65.2)	444 (62.8)	326 (64.9)	455 (63.6)	652 (65.1)	899 (63.2)
African Heritage / African American, n (%)	75 (15.0)	115 (16.3)	82 (16.3)	105 (14.7)	157 (15.7)	220 (15.5)
Other, n (%)	77 (15.4)	106 (15.0)	65 (12.9)	107 (15.0)	142 (14.2)	213 (15.0)

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = total number of subjects
n/% = number/percentage of subjects
SD = standard deviation
*Pid (b) (6) is 36 months of age and was included in the subgroup 18-35M

Table 54 History of influenza vaccination in the previous 3 seasons by age strata (Total vaccinated cohort)

		Q-QIV				F-QIV				Total			
		6-17M N = 500		18-35M N = 707		6-17M N = 502		18-35M N = 715		6-17M N = 1002		18-35M N = 1422	
Characteristics	**Parameters or Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one season	Yes	83	16.6	591	83.6	81	16.1	596	83.4	164	16.4	1187	83.5
	No	417	83.4	116	16.4	421	83.9	119	16.6	838	83.6	235	16.5
Season 2011-2012	Yes	0	0.0	8	1.1	0	0.0	13	1.8	0	0.0	21	1.5
Season 2012-2013	Yes	0	0.0	249	35.2	2	0.4	245	34.3	2	0.2	494	34.7
Season 2013-2014	Yes	83	16.6	541	76.5	79	15.7	540	75.5	162	16.2	1081	76.0

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = Total number of subjects
n= number of subjects with influenza vaccination during the specified season
% = n / Number of subjects with available results x 100

Table 55 Summary of demographic characteristics by priming status (Total vaccinated cohort)

		Q-QIV				F-QIV				Total			
		UNPRIM N = 550		PRIM N = 657		UNPRIM N = 560		PRIM N = 657		UNPRIM N = 1110		PRIM N = 1314	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	13.4	-	24.5	-	13.4	-	24.7	-	13.4	-	24.6	-
	SD	7.4	-	6.2	-	7.8	-	6.1	-	7.6	-	6.1	-
	Median	12.0	-	24.0	-	11.0	-	24.0	-	11.0	-	24.0	-
	Minimum	6	-	12	-	6	-	13	-	6	-	12	-
	Maximum	35	-	35	-	35	-	36*	-	35	-	36	-
Gender	Female	258	46.9	289	44.0	265	47.3	317	48.2	523	47.1	606	46.1
	Male	292	53.1	368	56.0	295	52.7	340	51.8	587	52.9	708	53.9
Ethnicity	American Hispanic or Latino	171	31.1	134	20.4	166	29.6	136	20.7	337	30.4	270	20.5
	Not American Hispanic or Latino	379	68.9	523	79.6	394	70.4	521	79.3	773	69.6	1044	79.5
Geographic Ancestry	African Heritage / African American	86	15.6	104	15.8	94	16.8	93	14.2	180	16.2	197	15.0
	American Indian or Alaskan Native	10	1.8	19	2.9	7	1.3	17	2.6	17	1.5	36	2.7
	Asian - Central/South Asian Heritage	2	0.4	2	0.3	3	0.5	6	0.9	5	0.5	8	0.6
	Asian - East Asian Heritage	1	0.2	2	0.3	2	0.4	3	0.5	3	0.3	5	0.4
	Asian - Japanese Heritage	0	0.0	1	0.2	0	0.0	2	0.3	0	0.0	3	0.2
	Asian - South East Asian Heritage	6	1.1	12	1.8	7	1.3	16	2.4	13	1.2	28	2.1
	Native Hawaiian or Other Pacific Islander	2	0.4	2	0.3	5	0.9	5	0.8	7	0.6	7	0.5
	White - Arabic / North African Heritage	3	0.5	2	0.3	1	0.2	3	0.5	4	0.4	5	0.4
	White - Caucasian / European Heritage	333	60.5	437	66.5	341	60.9	440	67.0	674	60.7	877	66.7
	Other	107	19.5	76	11.6	100	17.9	72	11.0	207	18.6	148	11.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation
*Pid (b) (6) is 36 months of age and was included in the subgroup 18-35M

Table 56 Summary of demographic characteristics by priming status (ATP cohort for immunogenicity)

		Q-QIV				F-QIV				Total			
		UNPRIM N = 426		PRIM N = 587		UNPRIM N = 442		PRIM N = 586		UNPRIM N = 868		PRIM N = 1173	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (months) at vaccination dose: 1	Mean	13.1	-	24.5	-	13.5	-	24.8	-	13.3	-	24.6	-
	SD	7.2	-	6.2	-	7.9	-	6.1	-	7.6	-	6.1	-
	Median	11.5	-	24.0	-	11.0	-	24.0	-	11.0	-	24.0	-
	Minimum	6	-	12	-	6	-	13	-	6	-	12	-
	Maximum	35	-	35	-	35	-	35	-	35	-	35	-
Gender	Female	198	46.5	264	45.0	213	48.2	283	48.3	411	47.4	547	46.6
	Male	228	53.5	323	55.0	229	51.8	303	51.7	457	52.6	626	53.4
Ethnicity	American Hispanic or Latino	132	31.0	117	19.9	140	31.7	122	20.8	272	31.3	239	20.4
	Not American Hispanic or Latino	294	69.0	470	80.1	302	68.3	464	79.2	596	68.7	934	79.6
Geographic Ancestry	African Heritage / African American	54	12.7	89	15.2	62	14.0	78	13.3	116	13.4	167	14.2
	American Indian or Alaskan Native	8	1.9	15	2.6	5	1.1	13	2.2	13	1.5	28	2.4
	Asian - Central/South Asian Heritage	2	0.5	2	0.3	2	0.5	6	1.0	4	0.5	8	0.7
	Asian - East Asian Heritage	1	0.2	1	0.2	2	0.5	2	0.3	3	0.3	3	0.3
	Asian - Japanese Heritage	0	0.0	1	0.2	0	0.0	2	0.3	0	0.0	3	0.3
	Asian - South East Asian Heritage	6	1.4	11	1.9	6	1.4	14	2.4	12	1.4	25	2.1
	Native Hawaiian or Other Pacific Islander	2	0.5	2	0.3	3	0.7	5	0.9	5	0.6	7	0.6
	White - Arabic / North African Heritage	3	0.7	2	0.3	1	0.2	3	0.5	4	0.5	5	0.4
	White - Caucasian / European Heritage	254	59.6	393	67.0	267	60.4	400	68.3	521	60.0	793	67.6
	Other	96	22.5	71	12.1	94	21.3	63	10.8	190	21.9	134	11.4

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Table 57 Age (in months) at vaccination Dose 1 by gender and by priming status (Total vaccinated cohort)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	UNPRIM	F	258	258	13.9	7.3	6	35
		M	292	292	12.9	7.4	6	35
		Total	550	550	13.4	7.4	6	35
	PRIM	F	289	289	24.4	6.1	12	35
		M	368	368	24.6	6.3	12	35
		Total	657	657	24.5	6.2	12	35
F-QIV*	UNPRIM	F	265	265	14.1	8.2	6	35
		M	295	295	12.8	7.3	6	35
		Total	560	560	13.4	7.8	6	35
	PRIM	F	317	317	24.7	6	14	36
		M	340	340	24.7	6.1	13	35
		Total	657	657	24.7	6.1	13	36
ALL	UNPRIM	F	523	523	14.0	7.8	6	35
		M	587	587	12.8	7.3	6	35
		Total	1110	1110	13.4	7.6	6	35
	PRIM	F	606	606	24.5	6.1	12	36
		M	708	708	24.6	6.2	12	35
		Total	1314	1314	24.6	6.1	12	36

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age
*Pid (b) (6) is 36 months of age and was included in the subgroup 18-35M

Table 58 Age (in months) at vaccination Dose 1 by gender and by priming status (ATP cohort for immunogenicity)

Group	Sub-group	Sex	N	N with age	MEAN	SD	MIN	MAX
Q-QIV	UNPRIM	F	198	198	13.4	7.1	6	34
		M	228	228	12.9	7.4	6	35
		Total	426	426	13.1	7.2	6	35
	PRIM	F	264	264	24.4	6.1	12	35
		M	323	323	24.5	6.2	12	35
		Total	587	587	24.5	6.2	12	35
F-QIV	UNPRIM	F	213	213	14.2	8.3	6	35
		M	229	229	12.8	7.5	6	35
		Total	442	442	13.5	7.9	6	35
	PRIM	F	283	283	24.7	6	14	35
		M	303	303	24.8	6.2	13	35
		Total	586	586	24.8	6.1	13	35
ALL	UNPRIM	F	411	411	13.9	7.7	6	35
		M	457	457	12.8	7.4	6	35
		Total	868	868	13.3	7.6	6	35
	PRIM	F	547	547	24.6	6.1	12	35
		M	626	626	24.7	6.2	12	35
		Total	1173	1173	24.6	6.1	12	35

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
F = female; M = male
N = number of subjects with documentation on gender
N with age = number of subjects with documentation on gender and age
SD = standard deviation
Min, Max = minimum, maximum age

Table 59 Summary of vital signs characteristics by priming status (Total vaccinated cohort)

		Q-QIV		F-QIV		Total	
		UNPRIM N = 550	PRIM N = 657	UNPRIM N = 560	PRIM N = 657	UNPRIM N = 1110	PRIM N = 1314
Characteristics	Parameters	Value	Value	Value	Value	Value	Value
Height (cm)	Mean	75.7	86.8	75.8	86.8	75.7	86.8
	SD	8.1	7.1	8.6	6.8	8.4	7.0
	Median	74.0	86.0	74.0	86.0	74.0	86.0
	Minimum	61.0	56.0	36.0	58.0	36.0	56.0
	Maximum	112.0	114.0	107.0	114.0	112.0	114.0
	Unknown	0	5	0	2	0	7
Weight (kg)	Mean	9.8	12.8	10.0	12.6	9.9	12.7
	SD	2.1	2.1	2.3	2.0	2.2	2.1
	Median	9.5	12.7	9.6	12.5	9.6	12.7
	Minimum	4.7	6.2	5.7	5.7	4.7	5.7
	Maximum	18.2	21.4	22.7	20.5	22.7	21.4
	Unknown	0	3	0	1	0	4

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation

Table 60 Study population by priming status (Total vaccinated cohort)

	Q-QIV		F-QIV		Total	
Number of subjects	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
Planned, N						
Randomised, N (Total Vaccinated Cohort)	550	657	560	657	1110	1314
Completed, n (%)	504 (91.6)	628 (95.6)	507 (90.5)	632 (96.2)	1011 (91.1)	1260 (95.9)
Demographics	UNPRIM	PRIM	UNPRIM	PRIM	UNPRIM	PRIM
N (Total Vaccinated Cohort)	550	657	560	657	1110	1314
Females:Males	258:292	289:368	265:295	317:340	523:587	606:708
Mean Age, months (SD)	13.4 (7.4)	24.5 (6.2)	13.4 (7.8)	24.7 (6.1)	13.4 (7.6)	24.6 (6.1)
Median Age, months (minimum, maximum)*	12 (6, 35)	24 (12, 35)	11 (6, 35)	24 (13, 36)	11 (6, 35)	24 (12, 36)
White - Caucasian / European Heritage, n (%)	333 (60.5)	437 (66.5)	341 (60.9)	440 (67.0)	674 (60.7)	877 (66.7)
African Heritage / African American, n (%)	86 (15.6)	104 (15.8)	94 (16.8)	93 (14.2)	180 (16.2)	197 (15.0)
Other, n (%)	107 (19.5)	76 (11.6)	100 (17.9)	72 (11.0)	207 (18.6)	148 (11.3)

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = total number of subjects
n/% = number/percentage of subjects
SD = standard deviation
*Pid (b) (6) is 36 months of age and was included in the subgroup 18-35M

Table 61 History of influenza vaccination in the previous 3 seasons by priming status (Total vaccinated cohort)

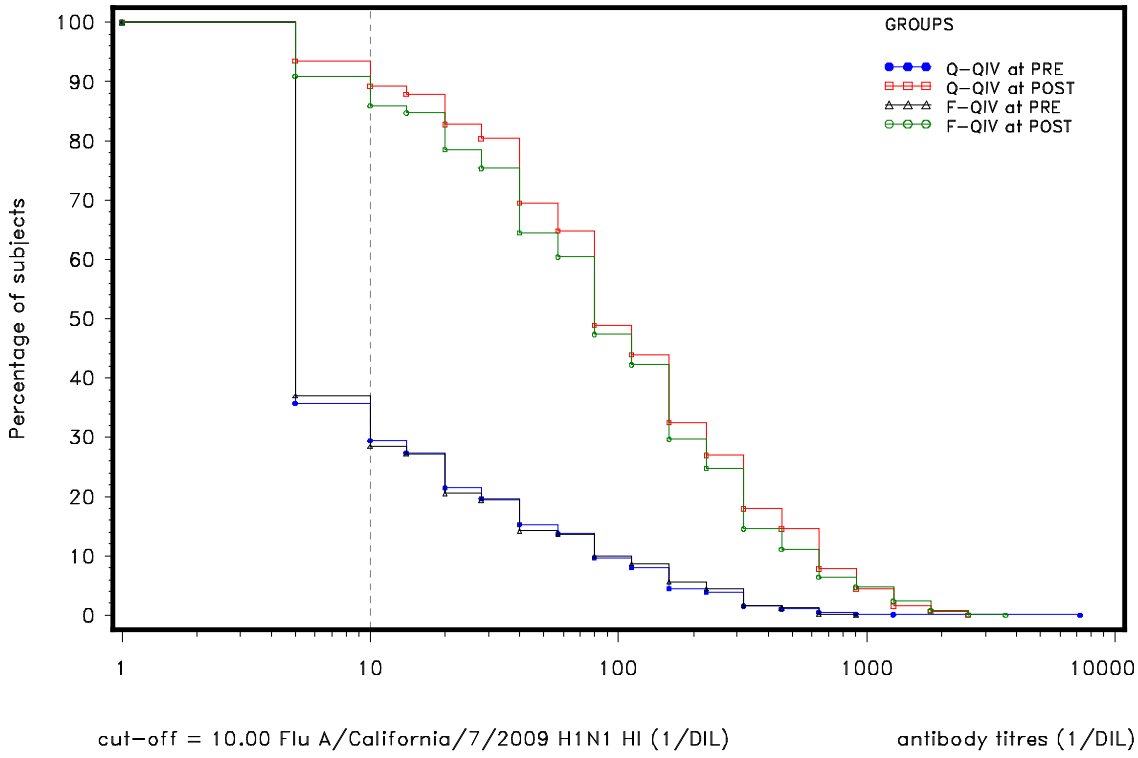
		Q-QIV				F-QIV				Total			
		UNPRIM N = 550		PRIM N = 657		UNPRIM N = 560		PRIM N = 657		UNPRIM N = 1110		PRIM N = 1314	
Characteristics	**Parameters or Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one season	Yes	17	3.1	657	100	20	3.6	657	100	37	3.3	1314	100
	No	533	96.9	0	0.0	540	96.4	0	0.0	1073	96.7	0	0.0
Season 2011-2012	Yes	0	0.0	8	1.2	1	0.2	12	1.8	1	0.1	20	1.5
Season 2012-2013	Yes	16	2.9	233	35.5	19	3.4	228	34.7	35	3.2	461	35.1
Season 2013-2014	Yes	1	0.2	623	94.8	0	0.0	619	94.2	1	0.1	1242	94.5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = Total number of subjects
n= number of subjects with influenza vaccination during the specified season
% = n / Number of subjects with available results x 100

10.2. Immunogenicity

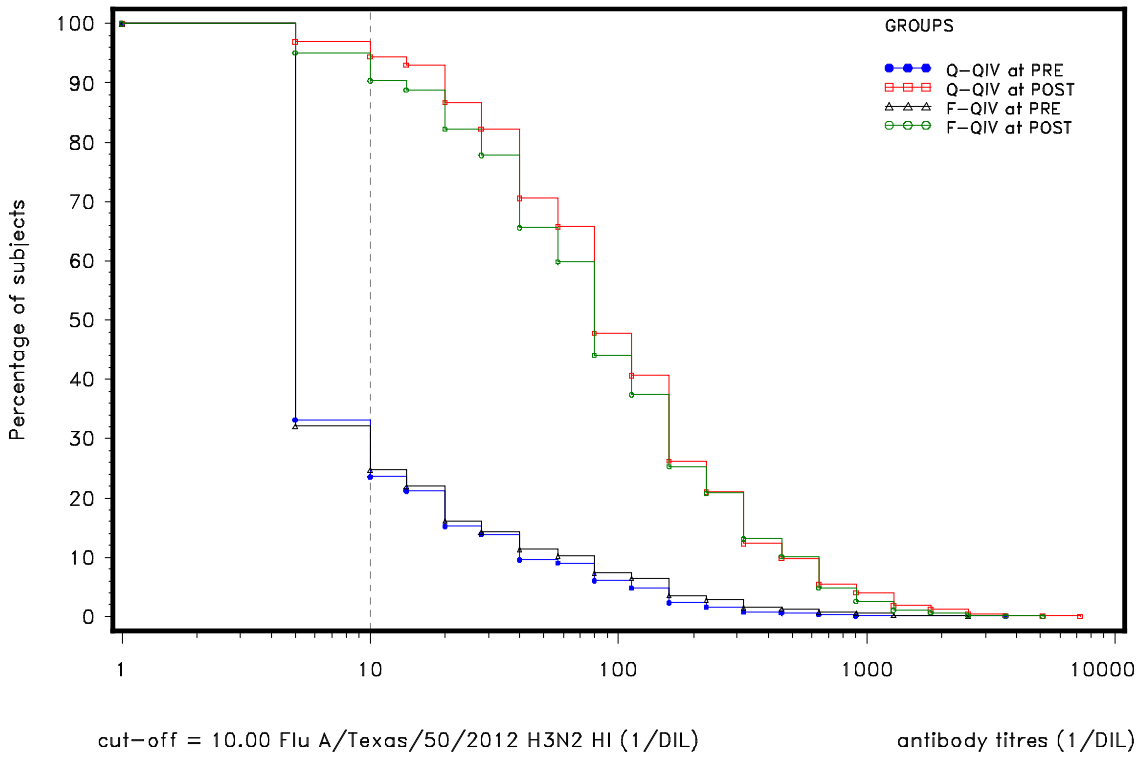
10.2.1. ATP cohort for Immunogenicity

Figure 1 Reverse cumulative distribution curve of Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)



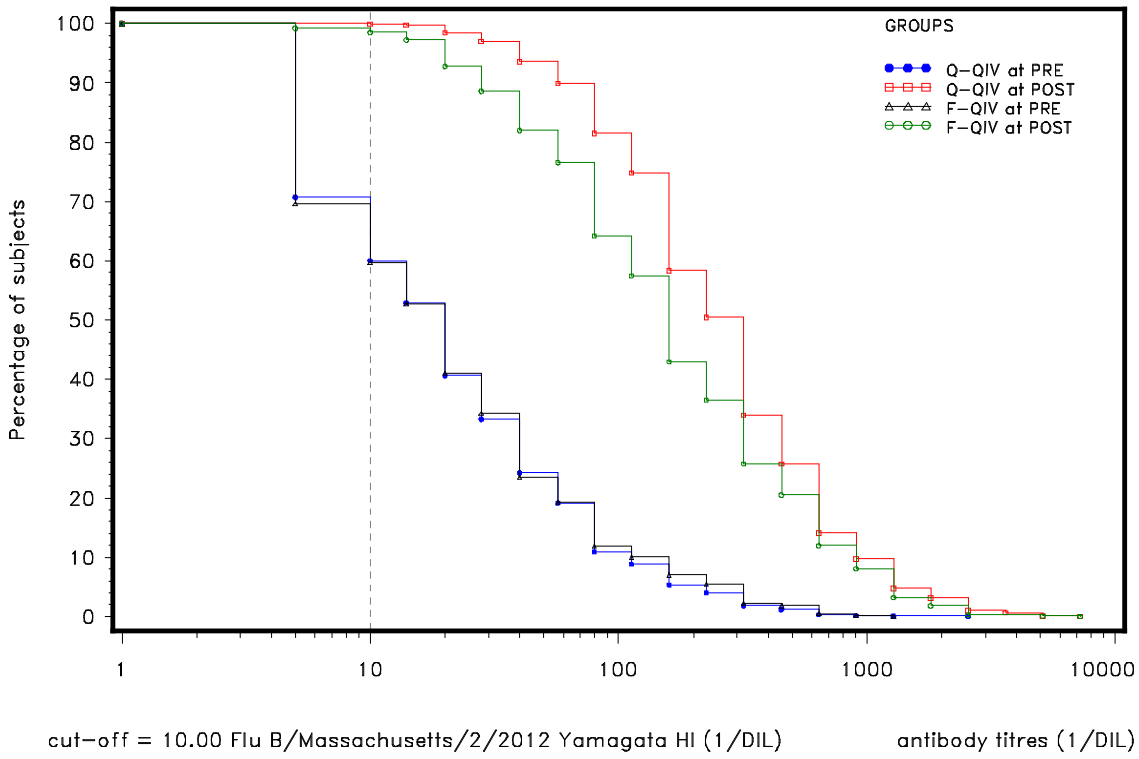
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Figure 2 **Reverse cumulative distribution curve of Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)**



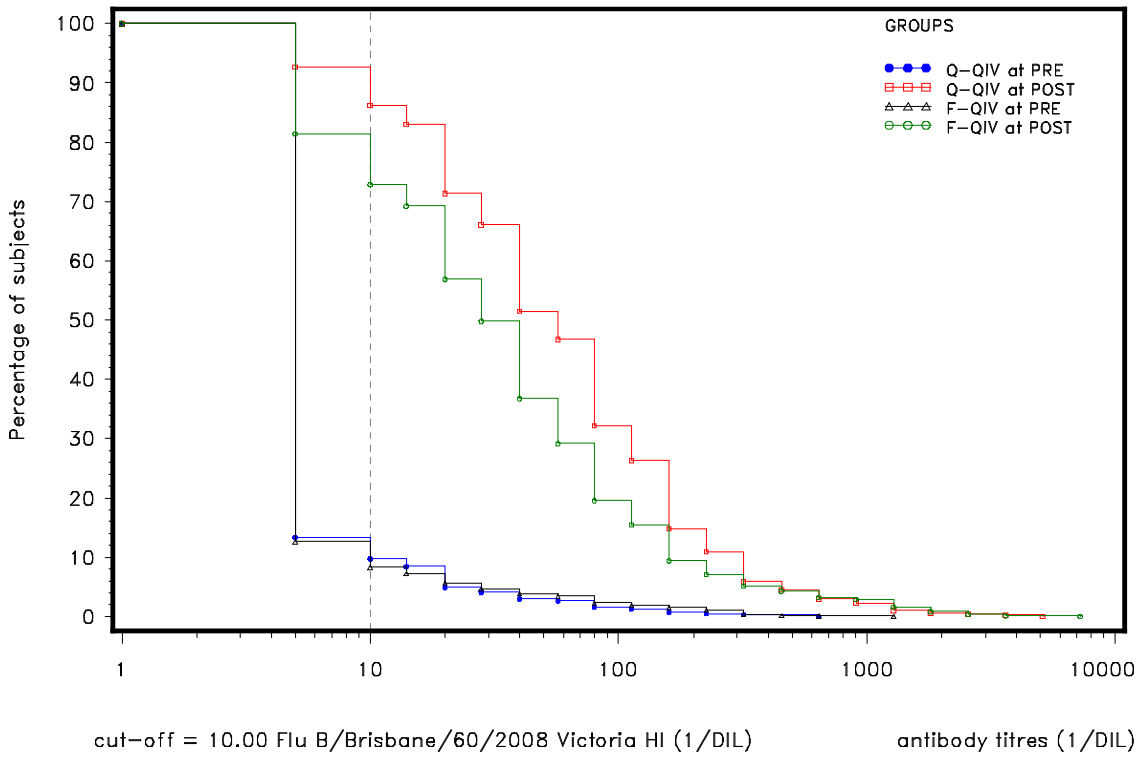
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Figure 3 **Reverse cumulative distribution curve of Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)**



Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Figure 4 **Reverse cumulative distribution curve of Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose (ATP cohort for immunogenicity)**



Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Table 62 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV/Q-QIV by age strata (6-17M) (ATP cohort for immunogenicity)

					Adjusted GMT ratio (F-QIV/6-17M / Q-QIV/6-17M)		
	F-QIV/6-17M		Q-QIV/6-17M			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
A/California/7/2009 (H1N1)	375	43.1	376	42.6	1.01	0.83	1.22
A/Texas/50/2012 (H3N2)	375	54.3	376	60.2	0.90	0.75	1.08
B/Massachusetts/2/2012 (Yamagata)	375	79.5	376	150.7	0.53	0.46	0.61
B/Brisbane/60/2008 (Victoria)	375	31.6	376	67.4	0.47	0.40	0.55

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 63 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV/Q-QIV by age strata (18-35M) (ATP cohort for immunogenicity)

					Adjusted GMT ratio (F-QIV/18-35M / Q-QIV/18-35M)		
	F-QIV/18-35M		Q-QIV/18-35M			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
A/California/7/2009 (H1N1)	605	130.0	596	169.8	0.77	0.69	0.85
A/Texas/50/2012 (H3N2)	605	111.9	596	136.4	0.82	0.73	0.92
B/Massachusetts/2/2012 (Yamagata)	605	268.3	598	358.2	0.75	0.68	0.82
B/Brisbane/60/2008 (Victoria)	605	35.2	597	47.5	0.74	0.65	0.85

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
18-35M = 18-35 months old subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 64 SCR Difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV minus Q-QIV by age strata (6-17M) (ATP cohort for immunogenicity)

							Difference in SCR (F-QIV/6-17M minus Q-QIV/6-17M)		
	F-QIV/6-17M			Q-QIV/6-17M				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
A/California/7/2009 (H1N1)	375	216	57.6	376	220	58.5	-0.91	-7.95	6.14
A/Texas/50/2012 (H3N2)	375	250	66.7	376	260	69.1	-2.48	-9.15	4.20
B/Brisbane/60/2008 (Victoria)	375	189	50.4	376	291	77.4	-26.99	-33.47	-20.29
B/Massachusetts/2/2012 (Yamagata)	375	232	61.9	376	299	79.5	-17.65	-23.99	-11.21

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 65 SCR Difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV minus Q-QIV by age strata (18-35M) (ATP cohort for immunogenicity)

							Difference in SCR (F-QIV/18-35M minus Q-QIV/18-35M)		
	F-QIV/18-35M			Q-QIV/18-35M				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
A/California/7/2009 (H1N1)	605	444	73.4	596	496	83.2	-9.83	-14.46	-5.19
A/Texas/50/2012 (H3N2)	605	430	71.1	596	480	80.5	-9.46	-14.27	-4.63
B/Brisbane/60/2008 (Victoria)	605	286	47.3	597	340	57.0	-9.68	-15.26	-4.03
B/Massachusetts/2/2012 (Yamagata)	605	491	81.2	598	534	89.3	-8.14	-12.16	-4.16

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
18-35M = 18-35 months old subjects
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 66 Flu A/California/7/2009 (H1N1) HI, A/Texas/50/2012 (H3N2) HI, B/Massachusetts/2/2012 (Yamagata) HI and B/Brisbane/60/2008 (Victoria) HI antibody parameters (Seropositivity rates, SPR, GMT, SCR, MGI) at Day 0 and 28 days after the last vaccine dose by age strata (ATP cohort for immunogenicity)

				N	≥10 1/DIL				SPR				GMT			N'	SCR				MGI		
							95%CI				95%CI			95%CI					95%CI			95%CI	
Antibody	Group	Sub-group	Timing		n''	%	LL	UL	n	%	LL	UL	Value	LL	UL		n'	%	LL	UL	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	6-17M	PRE	376	61	16.2	12.6	20.3	32	8.5	5.9	11.8	7.2	6.5	7.9	-	-						
			POST	400	343	85.8	81.9	89.0	245	61.3	56.3	66.1	42.7	37.1	49.0	376	220	58.5	53.3	63.5	6.0	5.3	6.8
		18-35M	PRE	596	286	48.0	43.9	52.1	159	26.7	23.2	30.4	14.5	13.0	16.2	-	-						
			POST	613	604	98.5	97.2	99.3	569	92.8	90.5	94.7	170.9	155.2	188.3	596	496	83.2	80.0	86.1	11.7	10.7	12.8
	F-QIV	6-17M	PRE	375	76	20.3	16.3	24.7	25	6.7	4.4	9.7	7.1	6.5	7.7	-	-						
			POST	401	332	82.8	78.7	86.4	240	59.9	54.9	64.7	43.2	37.3	50.0	375	216	57.6	52.4	62.7	6.1	5.2	7.1
		18-35M	PRE	605	287	47.4	43.4	51.5	165	27.3	23.8	31.0	14.6	13.1	16.4	-	-						
			POST	627	603	96.2	94.4	97.5	535	85.3	82.3	88.0	129.6	116.3	144.3	605	444	73.4	69.7	76.9	8.9	8.1	9.8
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	6-17M	PRE	376	41	10.9	7.9	14.5	12	3.2	1.7	5.5	5.8	5.5	6.1	-	-						
			POST	400	379	94.8	92.1	96.7	281	70.3	65.5	74.7	58.9	52.2	66.4	376	260	69.1	64.2	73.8	10.2	9.0	11.6
		18-35M	PRE	596	281	47.1	43.1	51.2	123	20.6	17.5	24.1	12.3	11.1	13.6	-	-						
			POST	613	603	98.4	97.0	99.2	552	90.0	87.4	92.3	136.0	123.7	149.6	596	480	80.5	77.1	83.6	11.1	10.1	12.1
	F-QIV	6-17M	PRE	375	53	14.1	10.8	18.1	15	4.0	2.3	6.5	6.2	5.8	6.7	-	-						
			POST	401	362	90.3	86.9	93.0	272	67.8	63.0	72.4	54.8	47.9	62.7	375	250	66.7	61.6	71.4	8.8	7.7	10.2
		18-35M	PRE	605	262	43.3	39.3	47.4	125	20.7	17.5	24.1	12.5	11.2	13.9	-	-						
			POST	627	616	98.2	96.9	99.1	528	84.2	81.1	87.0	111.1	100.6	122.7	605	430	71.1	67.3	74.7	9.0	8.2	9.9
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	6-17M	PRE	376	210	55.9	50.7	60.9	64	17.0	13.4	21.2	12.2	11.1	13.5	-	-						
			POST	400	400	100	99.1	100	377	94.3	91.5	96.3	151.0	137.4	165.9	376	299	79.5	75.1	83.5	12.3	10.7	14.3
		18-35M	PRE	598	479	80.1	76.7	83.2	260	43.5	39.5	47.6	28.0	25.2	31.0	-	-						
			POST	613	613	100	99.4	100	606	98.9	97.7	99.5	364.8	336.7	395.3	598	534	89.3	86.5	91.7	12.9	11.8	14.0
	F-QIV	6-17M	PRE	375	226	60.3	55.1	65.3	70	18.7	14.9	23.0	13.0	11.8	14.4	-	-						
			POST	401	397	99.0	97.5	99.7	311	77.6	73.2	81.5	79.1	70.9	88.1	375	232	61.9	56.7	66.8	6.1	5.3	7.0
		18-35M	PRE	605	457	75.5	71.9	78.9	266	44.0	40.0	48.0	27.4	24.5	30.7	-	-						
			POST	627	623	99.4	98.4	99.8	600	95.7	93.8	97.1	262.1	239.3	287.1	605	491	81.2	77.8	84.2	9.7	8.9	10.6
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	6-17M	PRE	376	28	7.4	5.0	10.6	2	0.5	0.1	1.9	5.5	5.3	5.7	-	-						
			POST	400	388	97.0	94.8	98.4	313	78.3	73.9	82.2	68.7	61.8	76.3	376	291	77.4	72.8	81.5	12.3	11.0	13.8
		18-35M	PRE	597	102	17.1	14.2	20.3	38	6.4	4.5	8.6	6.8	6.4	7.3	-	-						

				N	≥10 1/DIL				SPR				GMT			N'	SCR				MGI		
							95%CI				95%CI			95%CI					95%CI			95%CI	
Antibody	**Group**	**Sub-group**	**Timing**		**n''**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**Value**	**LL**	**UL**		**n'**	**%**	**LL**	**UL**	**Value**	**LL**	**UL**
			POST	613	551	89.9	87.2	92.2	356	58.1	54.1	62.0	47.8	42.6	53.6	597	340	57.0	52.9	61.0	7.0	6.4	7.7
	F-QIV	6-17M	PRE	375	27	7.2	4.8	10.3	7	1.9	0.8	3.8	5.6	5.3	5.9	-	-						
			POST	401	347	86.5	82.8	89.7	206	51.4	46.4	56.4	31.9	28.4	35.7	375	189	50.4	45.2	55.6	5.7	5.1	6.4
		18-35M	PRE	605	97	16.0	13.2	19.2	39	6.4	4.6	8.7	6.8	6.3	7.3	-	-						
			POST	627	490	78.1	74.7	81.3	306	48.8	44.8	52.8	34.4	30.4	38.8	605	286	47.3	43.2	51.3	5.2	4.7	5.7

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL at post-vaccination
For initially seropositive subjects, antibody titer at post-vaccination ≥ 4 fold the pre-vaccination antibody titer
GMT=geometric mean antibody titer calculated on all subjects
MGI=geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer
N =Number of subjects with results available (for seropositivity rates, SPR and GMT computation)
N'=Number of subjects with both pre and post results available (for SCR and MGI computation)
n''/%= number/percentage of subjects with titre equal to or above specified value
n/% = Number/percentage of seroprotected subjects
n'/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval: LL = Lower Limit UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Table 67 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV/Q-QIV by priming status (UNPRIMED) (ATP cohort for immunogenicity)

					Adjusted GMT ratio (F-QIV/UNPRIM / Q-QIV/UNPRIM)		
	F-QIV/UNPRIM		Q-QIV/UNPRIM			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
A/California/7/2009 (H1N1)	417	54.1	402	53.3	1.02	0.85	1.22
A/Texas/50/2012 (H3N2)	417	76.1	402	77.8	0.98	0.82	1.18
B/Massachusetts/2/2012 (Yamagata)	417	99.1	402	182.5	0.54	0.47	0.63
B/Brisbane/60/2008 (Victoria)	417	44.9	402	91.3	0.49	0.43	0.56

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 68 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV/Q-QIV by priming status (PRIMED) (ATP cohort for immunogenicity)

					Adjusted GMT ratio (F-QIV/PRIM / Q-QIV/PRIM)		
	F-QIV/PRIM		Q-QIV/PRIM			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
A/California/7/2009 (H1N1)	563	118.2	570	155.6	0.76	0.67	0.86
A/Texas/50/2012 (H3N2)	563	91.1	570	119.3	0.76	0.68	0.85
B/Massachusetts/2/2012 (Yamagata)	563	248.9	572	326.2	0.76	0.69	0.84
B/Brisbane/60/2008 (Victoria)	563	27.1	571	38.0	0.71	0.63	0.81

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
PRIM = Primed subjects
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 69 SCR Difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV minus Q-QIV by priming status (UNPRIMED) (ATP cohort for immunogenicity)

							Difference in SCR (F-QIV/UNPRIM minus Q-QIV/UNPRIM)		
	F-QIV/UNPRIM			Q-QIV/UNPRIM				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
A/California/7/2009 (H1N1)	417	264	63.3	402	257	63.9	-0.62	-7.20	5.97
A/Texas/50/2012 (H3N2)	417	302	72.4	402	296	73.6	-1.21	-7.28	4.88
B/Brisbane/60/2008 (Victoria)	417	259	62.1	402	357	88.8	-26.70	-32.25	-21.07
B/Massachusetts/2/2012 (Yamagata)	417	284	68.1	402	338	84.1	-15.97	-21.68	-10.21

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 70 SCR Difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV minus Q-QIV by priming status (PRIMED) (ATP cohort for immunogenicity)

							Difference in SCR (F-QIV/PRIM minus Q-QIV/PRIM)		
	F-QIV/PRIM			Q-QIV/PRIM				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
A/California/7/2009 (H1N1)	563	396	70.3	570	459	80.5	-10.19	-15.17	-5.19
A/Texas/50/2012 (H3N2)	563	378	67.1	570	444	77.9	-10.75	-15.90	-5.57
B/Brisbane/60/2008 (Victoria)	563	216	38.4	571	274	48.0	-9.62	-15.32	-3.86
B/Massachusetts/2/2012 (Yamagata)	563	439	78.0	572	495	86.5	-8.56	-13.01	-4.14

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
PRIM = Primed subjects
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 71 Flu A/California/7/2009 (H1N1) HI, A/Texas/50/2012 (H3N2) HI, B/Massachusetts/2/2012 (Yamagata) HI and B/Brisbane/60/2008 (Victoria) HI antibody parameters (Seropositivity rates, SPR, GMT, SCR, MGI) at Day 0 and 28 days after the last vaccine dose by priming status (ATP cohort for immunogenicity)

				N	≥10 1/DIL				SPR				GMT			N'	SCR				MGI		
							95%CI				95%CI			95%CI					95%CI			95%CI	
Antibody	Group	Sub-group	Timing		n''	%	LL	UL	n	%	LL	UL	Value	LL	UL		n'	%	LL	UL	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	UNPRIM	PRE	402	66	16.4	12.9	20.4	42	10.4	7.6	13.9	7.5	6.8	8.4	-	-						
			POST	426	371	87.1	83.5	90.1	282	66.2	61.5	70.7	51.4	44.7	59.1	402	257	63.9	59.0	68.6	6.9	6.1	7.8
		PRIM	PRE	570	281	49.3	45.1	53.5	149	26.1	22.6	30.0	14.4	12.9	16.1	-	-						
			POST	587	576	98.1	96.7	99.1	532	90.6	88.0	92.9	158.8	143.3	176.0	570	459	80.5	77.0	83.7	10.9	10.0	12.0
	F-QIV	UNPRIM	PRE	417	92	22.1	18.2	26.4	46	11.0	8.2	14.4	8.2	7.4	9.2	-	-						
			POST	442	381	86.2	82.6	89.3	294	66.5	61.9	70.9	56.0	48.4	64.8	417	264	63.3	58.5	67.9	6.8	5.9	7.8
		PRIM	PRE	563	271	48.1	43.9	52.4	144	25.6	22.0	29.4	13.8	12.3	15.4	-	-						
			POST	586	554	94.5	92.4	96.2	481	82.1	78.7	85.1	115.0	102.6	128.9	563	396	70.3	66.4	74.1	8.5	7.7	9.3
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	UNPRIM	PRE	402	46	11.4	8.5	15.0	27	6.7	4.5	9.6	6.4	5.9	7.0	-	-						
			POST	426	408	95.8	93.4	97.5	321	75.4	71.0	79.4	75.0	66.0	85.3	402	296	73.6	69.0	77.9	11.8	10.4	13.4
		PRIM	PRE	570	276	48.4	44.2	52.6	108	18.9	15.8	22.4	11.8	10.7	13.0	-	-						
			POST	587	574	97.8	96.2	98.8	512	87.2	84.2	89.8	118.4	107.5	130.3	570	444	77.9	74.3	81.2	10.0	9.1	10.9
	F-QIV	UNPRIM	PRE	417	60	14.4	11.2	18.1	31	7.4	5.1	10.4	6.9	6.3	7.6	-	-						
			POST	442	408	92.3	89.4	94.6	330	74.7	70.3	78.7	76.8	66.9	88.3	417	302	72.4	67.9	76.7	11.2	9.7	12.9
		PRIM	PRE	563	255	45.3	41.1	49.5	109	19.4	16.2	22.9	12.2	10.9	13.5	-	-						
			POST	586	570	97.3	95.6	98.4	470	80.2	76.7	83.4	90.4	81.8	100.0	563	378	67.1	63.1	71.0	7.6	6.9	8.3
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	UNPRIM	PRE	402	203	50.5	45.5	55.5	65	16.2	12.7	20.1	11.4	10.3	12.6	-	-						
			POST	426	426	100	99.1	100	407	95.5	93.1	97.3	179.8	163.7	197.4	402	338	84.1	80.1	87.5	16.0	13.9	18.5
		PRIM	PRE	572	486	85.0	81.8	87.8	259	45.3	41.1	49.5	30.5	27.6	33.8	-	-						
			POST	587	587	100	99.4	100	576	98.1	96.7	99.1	334.3	306.4	364.7	572	495	86.5	83.5	89.2	10.7	9.9	11.6
	F-QIV	UNPRIM	PRE	417	220	52.8	47.8	57.6	80	19.2	15.5	23.3	12.4	11.2	13.7	-	-						
			POST	442	439	99.3	98.0	99.9	362	81.9	78.0	85.4	98.1	88.1	109.3	417	284	68.1	63.4	72.6	8.0	6.9	9.3
		PRIM	PRE	563	463	82.2	78.8	85.3	256	45.5	41.3	49.7	30.1	27.0	33.6	-	-						
			POST	586	581	99.1	98.0	99.7	549	93.7	91.4	95.5	242.2	219.1	267.7	563	439	78.0	74.3	81.3	8.2	7.6	8.9

				N	≥10 1/DIL				SPR				GMT			N'	SCR				MGI		
							95%CI				95%CI			95%CI					95%CI			95%CI	
Antibody	**Group**	**Sub-group**	**Timing**		**n''**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**Value**	**LL**	**UL**		**n'**	**%**	**LL**	**UL**	**Value**	**LL**	**UL**
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	UNPRIM	PRE	402	28	7.0	4.7	9.9	9	2.2	1.0	4.2	5.6	5.3	5.9	-	-						
			POST	426	422	99.1	97.6	99.7	379	89.0	85.6	91.8	91.7	83.8	100.3	402	357	88.8	85.3	91.7	16.2	14.8	17.8
		PRIM	PRE	571	102	17.9	14.8	21.3	31	5.4	3.7	7.6	6.7	6.3	7.2	-	-						
			POST	587	517	88.1	85.2	90.6	290	49.4	45.3	53.5	38.1	34.0	42.8	571	274	48.0	43.8	52.2	5.6	5.1	6.1
	F-QIV	UNPRIM	PRE	417	27	6.5	4.3	9.3	11	2.6	1.3	4.7	5.6	5.3	6.0	-	-						
			POST	442	409	92.5	89.7	94.8	277	62.7	58.0	67.2	44.8	40.1	50.0	417	259	62.1	57.3	66.8	8.0	7.2	8.8
		PRIM	PRE	563	97	17.2	14.2	20.6	35	6.2	4.4	8.5	6.8	6.4	7.3	-	-						
			POST	586	428	73.0	69.2	76.6	235	40.1	36.1	44.2	26.7	23.6	30.3	563	216	38.4	34.3	42.5	4.0	3.6	4.4

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL at post-vaccination
For initially seropositive subjects, antibody titer at post-vaccination ≥ 4 fold the pre-vaccination antibody titer
GMT=geometric mean antibody titer calculated on all subjects
MGI=geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer
N =Number of subjects with results available (for seropositivity rates, SPR and GMT computation)
N'=Number of subjects with both pre and post results available (for SCR and MGI computation)
n''/%= number/percentage of subjects with titre equal to or above specified value
n/% = Number/percentage of seroprotected subjects
n'/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval: LL = Lower Limit UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

10.2.2. TVC for Immunogenicity

Table 72 Adjusted GMT ratios of A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV/Q-QIV (Total vaccinated cohort)

					Adjusted GMT ratio (F-QIV / Q-QIV)		
	F-QIV		Q-QIV			95% CI	
Antibody	N	Adjusted GMT	N	Adjusted GMT	Value	LL	UL
A/California/7/2009 (H1N1)	1037	83.8	1036	98.2	0.85	0.77	0.94
A/Texas/50/2012 (H3N2)	1037	83.7	1036	100.6	0.83	0.75	0.92
B/Massachusetts/2/2012 (Yamagata)	1037	163.5	1038	256.4	0.64	0.58	0.70
B/Brisbane/60/2008 (Victoria)	1037	33.6	1037	55.5	0.61	0.55	0.67

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Adjusted GMT = geometric mean antibody titre adjusted for baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for baseline titre - pooled variance); LL = lower limit, UL = upper limit

Table 73 SCR Difference between groups for A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at 28 days after the last vaccine dose: F-QIV minus Q-QIV (Total vaccinated cohort)

							Difference in SCR (F-QIV minus Q-QIV)		
	F-QIV			Q-QIV				95% CI	
Antibody	N	n	%	N	n	%	%	LL	UL
A/California/7/2009 (H1N1)	1037	693	66.8	1036	760	73.4	-6.53	-10.46	-2.59
A/Texas/50/2012 (H3N2)	1037	714	68.9	1036	792	76.4	-7.60	-11.41	-3.76
B/Brisbane/60/2008 (Victoria)	1037	503	48.5	1037	677	65.3	-16.78	-20.95	-12.55
B/Massachusetts/2/2012 (Yamagata)	1037	764	73.7	1038	888	85.5	-11.88	-15.31	-8.44

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
SCR defined as:
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects with a vaccine response
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit

Table 74 Seroconversion rate (SCR) for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) 28 days after the last vaccine dose for FLU Q-QIV and FLU F-QIV (Total vaccinated cohort)

			SCR			
					95% CI	
Antibody	**Group**	**N**	**n**	**%**	**LL**	**UL**
A/California/7/2009 (H1N1)	Q-QIV	1036	760	73.4	70.6	76.0
	F-QIV	1037	693	66.8	63.9	69.7
A/Texas/50/2012 (H3N2)	Q-QIV	1036	792	76.4	73.7	79.0
	F-QIV	1037	714	68.9	65.9	71.7
B/Massachusetts/2/2012 (Yamagata)	Q-QIV	1038	888	85.5	83.3	87.6
	F-QIV	1037	764	73.7	70.9	76.3
B/Brisbane/60/2008 (Victoria)	Q-QIV	1037	677	65.3	62.3	68.2
	F-QIV	1037	503	48.5	45.4	51.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
SCR defined as :
For initially seronegative subjects, antibody titre ≥ 40 1/DIL after vaccination
For initially seropositive subjects antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of seroconverted subjects
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 75 Flu A/California/7/2009 (H1N1) HI, A/Texas/50/2012 (H3N2) HI, B/Massachusetts/2/2012 (Yamagata) HI and B/Brisbane/60/2008 (Victoria) HI antibody parameters (Seropositivity rates, SPR, GMT, SCR, MGI) at Day 0 and 28 days after the last vaccine dose (Total vaccinated cohort)

			N	≥10 1/DIL				SPR				GMT			N'	SCR				MGI		
						95%CI				95%CI			95%CI					95%CI			95%CI	
Antibody	Group	Timing		n''	%	LL	UL	n	%	LL	UL	Value	LL	UL		n'	%	LL	UL	Value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	PRE	1139	401	35.2	32.4	38.1	225	19.8	17.5	22.2	11.1	10.3	11.9	-	-						
		POST	1080	1010	93.5	91.9	94.9	863	79.9	77.4	82.3	97.1	89.0	106.0	1036	760	73.4	70.6	76.0	8.9	8.3	9.6
	F-QIV	PRE	1140	421	36.9	34.1	39.8	225	19.7	17.5	22.2	11.2	10.4	12.0	-	-						
		POST	1088	985	90.5	88.6	92.2	817	75.1	72.4	77.6	83.1	75.9	91.0	1037	693	66.8	63.9	69.7	7.6	7.0	8.2
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	PRE	1139	364	32.0	29.3	34.8	152	13.3	11.4	15.5	9.1	8.5	9.6	-	-						
		POST	1080	1049	97.1	96.0	98.0	890	82.4	80.0	84.6	98.1	91.0	105.9	1036	792	76.4	73.7	79.0	10.9	10.1	11.7
	F-QIV	PRE	1140	361	31.7	29.0	34.5	159	13.9	12.0	16.1	9.5	8.9	10.2	-	-						
		POST	1088	1037	95.3	93.9	96.5	843	77.5	74.9	79.9	84.0	77.5	91.0	1037	714	68.9	65.9	71.7	8.9	8.2	9.6
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	PRE	1141	789	69.1	66.4	71.8	368	32.3	29.5	35.1	19.6	18.3	21.1	-	-						
		POST	1080	1080	100	99.7	100	1048	97.0	95.8	98.0	254.7	238.9	271.6	1038	888	85.5	83.3	87.6	12.9	12.0	13.9
	F-QIV	PRE	1140	784	68.8	66.0	71.5	376	33.0	30.3	35.8	19.8	18.4	21.3	-	-						
		POST	1088	1079	99.2	98.4	99.6	962	88.4	86.4	90.3	161.7	149.8	174.6	1037	764	73.7	70.9	76.3	8.1	7.5	8.8
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	PRE	1140	150	13.2	11.2	15.3	46	4.0	3.0	5.3	6.2	6.0	6.5	-	-						
		POST	1080	1005	93.1	91.4	94.5	719	66.6	63.7	69.4	56.4	52.1	61.1	1037	677	65.3	62.3	68.2	8.8	8.2	9.5
	F-QIV	PRE	1140	145	12.7	10.8	14.8	54	4.7	3.6	6.1	6.3	6.0	6.6	-	-						
		POST	1088	884	81.3	78.8	83.5	542	49.8	46.8	52.8	33.2	30.5	36.2	1037	503	48.5	45.4	51.6	5.4	5.0	5.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Seroconversion defined as:
For initially seronegative subjects, antibody titer ≥ 40 1/DIL at post-vaccination
For initially seropositive subjects, antibody titer at post-vaccination ≥ 4 fold the pre-vaccination antibody titer
GMT=geometric mean antibody titer calculated on all subjects
MGI=geometric mean of the within-subject ratios of the post-vaccination reciprocal HI titer to the Day 0 reciprocal HI titer
N =Number of subjects with results available (for seropositivity rates, SPR and GMT computation)
N'=Number of subjects with both pre and post results available (for SCR and MGI computation)
n''/%= number/percentage of subjects with titre equal to or above specified value
n/% = Number/percentage of seroprotected subjects
n'/% = Number/percentage of seroconverted subjects
95% CI = 95% confidence interval: LL = Lower Limit UL = Upper Limit

PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

10.2.3. Exploratory immunogenicity analysis (potential impact of vaccine stability)

Table 76 Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by vaccination date (ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group*	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	OCT2014	PRE	345	165	47.8	42.4	53.2	13.1	11.4	14.9
			POST	355	350	98.6	96.7	99.5	141.1	124.0	160.4
		NOV2014	PRE	322	124	38.5	33.2	44.1	12.9	11.0	15.2
			POST	339	314	92.6	89.3	95.2	108.5	91.9	128.1
		DEC2014	PRE	215	43	20.0	14.9	26.0	7.9	6.9	9.2
			POST	227	196	86.3	81.2	90.5	62.8	51.3	76.9
		JAN2015	PRE	90	15	16.7	9.6	26.0	7.2	5.9	8.7
			POST	92	87	94.6	87.8	98.2	54.3	41.7	70.5
	F-QIV	OCT2014	PRE	346	170	49.1	43.7	54.5	14.5	12.5	16.7
			POST	359	341	95.0	92.2	97.0	115.0	99.7	132.7
		NOV2014	PRE	325	121	37.2	32.0	42.7	10.6	9.3	12.2
			POST	345	302	87.5	83.6	90.8	72.2	60.8	85.7
		DEC2014	PRE	218	50	22.9	17.5	29.1	8.6	7.3	10.1
			POST	233	211	90.6	86.1	94.0	73.5	60.5	89.2
		JAN2015	PRE	91	22	24.2	15.8	34.3	8.4	6.6	10.8
			POST	91	81	89.0	80.7	94.6	64.2	46.5	88.5
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	OCT2014	PRE	345	168	48.7	43.3	54.1	11.3	10.0	12.7
			POST	355	346	97.5	95.2	98.8	108.3	96.1	121.9
		NOV2014	PRE	322	101	31.4	26.3	36.7	8.9	7.9	9.9
			POST	339	329	97.1	94.6	98.6	97.2	85.2	110.9
		DEC2014	PRE	215	40	18.6	13.6	24.5	7.8	6.7	9.1
			POST	227	217	95.6	92.0	97.9	81.3	67.8	97.5
		JAN2015	PRE	90	13	14.4	7.9	23.4	7.0	5.7	8.4
			POST	92	90	97.8	92.4	99.7	105.7	76.4	146.3
	F-QIV	OCT2014	PRE	346	157	45.4	40.0	50.8	12.2	10.7	13.9
			POST	359	347	96.7	94.2	98.3	88.7	78.4	100.3
		NOV2014	PRE	325	93	28.6	23.8	33.9	8.7	7.7	9.8
			POST	345	320	92.8	89.5	95.3	66.5	57.6	76.8
		DEC2014	PRE	218	43	19.7	14.7	25.6	7.8	6.7	9.0
			POST	233	225	96.6	93.3	98.5	95.2	79.2	114.5
		JAN2015	PRE	91	22	24.2	15.8	34.3	9.0	6.8	11.9
			POST	91	86	94.5	87.6	98.2	124.9	90.0	173.4
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	OCT2014	PRE	346	293	84.7	80.4	88.3	30.5	26.7	34.7
			POST	355	355	100	99.0	100	319.1	285.5	356.5
		NOV2014	PRE	323	220	68.1	62.7	73.2	19.1	16.6	21.9
			POST	339	339	100	98.9	100	253.7	226.3	284.5
		DEC2014	PRE	215	130	60.5	53.6	67.0	14.6	12.5	17.1
			POST	227	227	100	98.4	100	204.9	178.3	235.5
		JAN2015	PRE	90	46	51.1	40.3	61.8	11.8	9.3	14.9
			POST	92	92	100	96.1	100	209.1	167.3	261.3

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group***	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
	F-QIV	OCT2014	PRE	346	287	82.9	78.6	86.8	31.2	27.1	35.9
			POST	359	357	99.4	98.0	99.9	248.3	219.5	280.8
		NOV2014	PRE	325	240	73.8	68.7	78.5	21.2	18.6	24.3
			POST	345	343	99.4	97.9	99.9	143.1	124.2	164.8
		DEC2014	PRE	218	115	52.8	45.9	59.5	13.8	11.7	16.3
			POST	233	229	98.3	95.7	99.5	125.1	107.1	146.1
		JAN2015	PRE	91	41	45.1	34.6	55.8	10.2	8.3	12.5
			POST	91	91	100	96.0	100	108.9	84.8	139.8
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	OCT2014	PRE	345	65	18.8	14.9	23.4	6.6	6.1	7.2
			POST	355	317	89.3	85.6	92.3	40.3	34.7	46.8
		NOV2014	PRE	323	36	11.1	7.9	15.1	6.2	5.7	6.7
			POST	339	311	91.7	88.3	94.4	57.8	50.0	66.8
		DEC2014	PRE	215	19	8.8	5.4	13.5	5.9	5.4	6.3
			POST	227	220	96.9	93.7	98.8	67.5	58.7	77.6
		JAN2015	PRE	90	10	11.1	5.5	19.5	6.0	5.3	6.9
			POST	92	91	98.9	94.1	100	94.4	76.8	116.0
	F-QIV	OCT2014	PRE	346	63	18.2	14.3	22.7	6.8	6.3	7.5
			POST	359	271	75.5	70.7	79.9	28.7	24.5	33.7
		NOV2014	PRE	325	39	12.0	8.7	16.0	6.1	5.6	6.5
			POST	345	282	81.7	77.3	85.7	31.3	27.1	36.2
		DEC2014	PRE	218	17	7.8	4.6	12.2	6.0	5.4	6.6
			POST	233	201	86.3	81.2	90.4	39.6	33.5	46.8
		JAN2015	PRE	91	5	5.5	1.8	12.4	5.9	5.0	6.8
			POST	91	83	91.2	83.4	96.1	49.7	38.1	64.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
*= Time window was classified according to subjects' last dose date
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Table 77 Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by vaccination date for primed subjects (ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group*	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	OCT2014	PRE	334	163	48.8	43.3	54.3	13.3	11.6	15.2
			POST	344	339	98.5	96.6	99.5	143.4	125.9	163.2
		NOV2014	PRE	169	91	53.8	46.0	61.5	18.2	14.4	22.9
			POST	175	171	97.7	94.3	99.4	187.1	153.1	228.7
		DEC2014	PRE	67	27	40.3	28.5	53.0	12.3	8.9	17.0
			POST	68	66	97.1	89.8	99.6	174.5	128.8	236.3
	F-QIV	OCT2014	PRE	334	166	49.7	44.2	55.2	14.6	12.6	16.8
			POST	347	332	95.7	93.0	97.6	117.2	101.6	135.0
		NOV2014	PRE	169	81	47.9	40.2	55.7	13.1	10.8	16.0
			POST	177	165	93.2	88.5	96.4	109.8	88.0	137.1
		DEC2014	PRE	59	23	39.0	26.5	52.6	11.7	8.2	16.7
			POST	61	56	91.8	81.9	97.3	117.0	78.6	174.0
		JAN2015	PRE	1	1	100	2.5	100	10.0	-	-
			POST	1	1	100	2.5	100	226.0	-	-
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	OCT2014	PRE	334	166	49.7	44.2	55.2	11.6	10.2	13.1
			POST	344	335	97.4	95.1	98.8	109.2	96.9	123.1
		NOV2014	PRE	169	84	49.7	41.9	57.5	12.2	10.3	14.5
			POST	175	171	97.7	94.3	99.4	126.6	104.6	153.2
		DEC2014	PRE	67	26	38.8	27.1	51.5	12.2	8.4	17.5
			POST	68	68	100	94.7	100	149.6	112.0	199.8
	F-QIV	OCT2014	PRE	334	154	46.1	40.7	51.6	12.3	10.8	14.1
			POST	347	336	96.8	94.4	98.4	89.2	78.7	101.2
		NOV2014	PRE	169	78	46.2	38.5	54.0	12.1	10.0	14.7
			POST	177	173	97.7	94.3	99.4	90.8	75.0	110.0
		DEC2014	PRE	59	22	37.3	25.0	50.9	10.7	7.5	15.2
			POST	61	60	98.4	91.2	100	92.8	66.2	130.0
		JAN2015	PRE	1	1	100	2.5	100	1280.0	-	-
			POST	1	1	100	2.5	100	905.0	-	-
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	OCT2014	PRE	335	289	86.3	82.1	89.8	31.9	28.0	36.4
			POST	344	344	100	98.9	100	323.6	289.2	361.9
		NOV2014	PRE	170	139	81.8	75.1	87.3	29.9	24.5	36.5
			POST	175	175	100	97.9	100	338.9	286.8	400.5
		DEC2014	PRE	67	58	86.6	76.0	93.7	25.6	19.2	34.1
			POST	68	68	100	94.7	100	380.6	294.8	491.3
	F-QIV	OCT2014	PRE	334	279	83.5	79.1	87.3	31.8	27.6	36.7
			POST	347	345	99.4	97.9	99.9	254.6	224.5	288.8
		NOV2014	PRE	169	141	83.4	77.0	88.7	29.5	24.4	35.8
			POST	177	175	98.9	96.0	99.9	243.2	201.2	294.0
		DEC2014	PRE	59	42	71.2	57.9	82.2	23.3	16.0	33.9
			POST	61	60	98.4	91.2	100	177.1	126.5	248.0
		JAN2015	PRE	1	1	100	2.5	100	28.0	-	-
			POST	1	1	100	2.5	100	640.0	-	-

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group***	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	OCT2014	PRE	334	65	19.5	15.4	24.1	6.7	6.2	7.2
			POST	344	306	89.0	85.2	92.1	39.2	33.7	45.6
		NOV2014	PRE	170	26	15.3	10.2	21.6	6.8	6.0	7.7
			POST	175	150	85.7	79.6	90.5	35.0	28.3	43.3
		DEC2014	PRE	67	11	16.4	8.5	27.5	6.7	5.6	8.1
			POST	68	61	89.7	79.9	95.8	41.4	29.5	58.3
	F-QIV	OCT2014	PRE	334	63	18.9	14.8	23.5	6.9	6.3	7.6
			POST	347	260	74.9	70.0	79.4	28.1	23.9	33.2
		NOV2014	PRE	169	29	17.2	11.8	23.7	6.8	6.0	7.7
			POST	177	128	72.3	65.1	78.8	26.7	21.2	33.6
		DEC2014	PRE	59	5	8.5	2.8	18.7	6.3	5.0	7.9
			POST	61	40	65.6	52.3	77.3	20.6	14.4	29.4
		JAN2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	0	0.0	0.0	97.5	5.0	-	-

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
*= Time window was classified according to subjects' last dose date
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

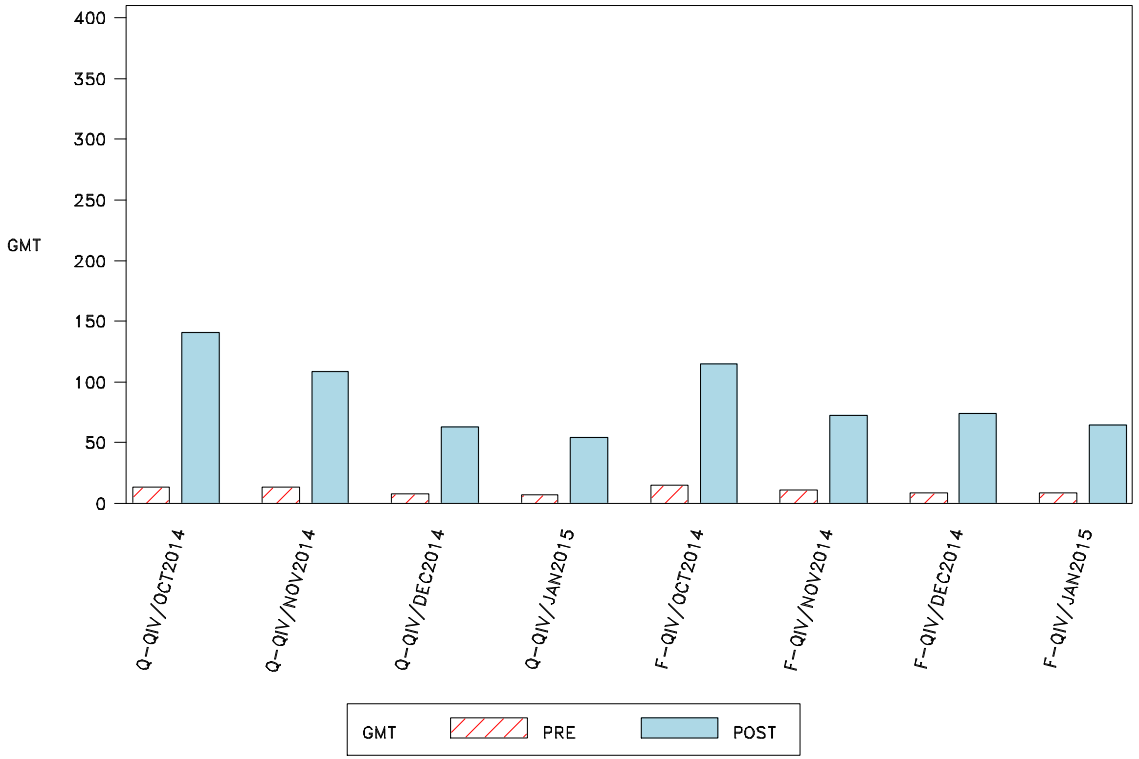
Table 78 Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by vaccination date for unprimed subjects (ATP cohort for immunogenicity)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group*	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	OCT2014	PRE	11	2	18.2	2.3	51.8	7.8	3.9	15.5
			POST	11	11	100	71.5	100	85.1	32.8	220.9
		NOV2014	PRE	153	33	21.6	15.3	28.9	8.9	7.3	10.9
			POST	164	143	87.2	81.1	91.9	60.6	47.7	77.1
		DEC2014	PRE	148	16	10.8	6.3	17.0	6.5	5.6	7.5
			POST	159	130	81.8	74.9	87.4	40.6	32.4	50.9
		JAN2015	PRE	90	15	16.7	9.6	26.0	7.2	5.9	8.7
			POST	92	87	94.6	87.8	98.2	54.3	41.7	70.5
	F-QIV	OCT2014	PRE	12	4	33.3	9.9	65.1	12.6	4.5	35.4
			POST	12	9	75.0	42.8	94.5	67.3	17.7	255.1
		NOV2014	PRE	156	40	25.6	19.0	33.2	8.5	7.1	10.1
			POST	168	137	81.5	74.8	87.1	46.4	36.1	59.6
		DEC2014	PRE	159	27	17.0	11.5	23.7	7.7	6.4	9.1
			POST	172	155	90.1	84.6	94.1	62.3	50.1	77.5
		JAN2015	PRE	90	21	23.3	15.1	33.4	8.4	6.5	10.8
			POST	90	80	88.9	80.5	94.5	63.3	45.7	87.5
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	OCT2014	PRE	11	2	18.2	2.3	51.8	5.7	4.7	6.8
			POST	11	11	100	71.5	100	82.4	31.6	214.8
		NOV2014	PRE	153	17	11.1	6.6	17.2	6.2	5.5	7.0
			POST	164	158	96.3	92.2	98.6	73.4	61.8	87.1
		DEC2014	PRE	148	14	9.5	5.3	15.4	6.4	5.6	7.4
			POST	159	149	93.7	88.7	96.9	62.6	50.4	77.8
		JAN2015	PRE	90	13	14.4	7.9	23.4	7.0	5.7	8.4
			POST	92	90	97.8	92.4	99.7	105.7	76.4	146.3
	F-QIV	OCT2014	PRE	12	3	25.0	5.5	57.2	8.7	4.2	17.8
			POST	12	11	91.7	61.5	99.8	73.4	35.0	153.7
		NOV2014	PRE	156	15	9.6	5.5	15.4	6.0	5.4	6.8
			POST	168	147	87.5	81.5	92.1	47.9	39.0	58.8
		DEC2014	PRE	159	21	13.2	8.4	19.5	6.9	6.0	8.1
			POST	172	165	95.9	91.8	98.3	96.1	77.0	119.9
		JAN2015	PRE	90	21	23.3	15.1	33.4	8.5	6.5	11.1
			POST	90	85	94.4	87.5	98.2	122.2	87.9	169.8
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	OCT2014	PRE	11	4	36.4	10.9	69.2	7.3	4.9	10.8
			POST	11	11	100	71.5	100	205.8	90.0	470.7
		NOV2014	PRE	153	81	52.9	44.7	61.1	11.6	9.9	13.5
			POST	164	164	100	97.8	100	186.3	161.5	215.0
		DEC2014	PRE	148	72	48.6	40.4	57.0	11.3	9.5	13.5
			POST	159	159	100	97.7	100	157.2	135.5	182.5
		JAN2015	PRE	90	46	51.1	40.3	61.8	11.8	9.3	14.9
			POST	92	92	100	96.1	100	209.1	167.3	261.3
	F-QIV	OCT2014	PRE	12	8	66.7	34.9	90.1	17.3	8.3	36.1
			POST	12	12	100	73.5	100	119.9	76.6	187.7
		NOV2014	PRE	156	99	63.5	55.4	71.0	14.9	12.5	17.6
			POST	168	168	100	97.8	100	81.8	68.6	97.6

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group***	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
		DEC2014	PRE	159	73	45.9	38.0	54.0	11.3	9.5	13.5
			POST	172	169	98.3	95.0	99.6	110.6	93.2	131.3
		JAN2015	PRE	90	40	44.4	34.0	55.3	10.1	8.2	12.3
			POST	90	90	100	96.0	100	106.7	83.1	137.0
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	OCT2014	PRE	11	0	0.0	0.0	28.5	5.0	5.0	5.0
			POST	11	11	100	71.5	100	99.7	49.8	199.5
		NOV2014	PRE	153	10	6.5	3.2	11.7	5.6	5.1	6.1
			POST	164	161	98.2	94.7	99.6	98.6	84.0	115.7
		DEC2014	PRE	148	8	5.4	2.4	10.4	5.5	5.1	6.0
			POST	159	159	100	97.7	100	83.2	73.5	94.2
		JAN2015	PRE	90	10	11.1	5.5	19.5	6.0	5.3	6.9
			POST	92	91	98.9	94.1	100	94.4	76.8	116.0
	F-QIV	OCT2014	PRE	12	0	0.0	0.0	26.5	5.0	5.0	5.0
			POST	12	11	91.7	61.5	99.8	50.4	25.5	99.4
		NOV2014	PRE	156	10	6.4	3.1	11.5	5.4	5.1	5.7
			POST	168	154	91.7	86.4	95.4	37.1	31.3	44.1
		DEC2014	PRE	159	12	7.5	4.0	12.8	5.8	5.3	6.5
			POST	172	161	93.6	88.8	96.8	49.9	41.8	59.6
		JAN2015	PRE	90	5	5.6	1.8	12.5	5.9	5.0	6.8
			POST	90	83	92.2	84.6	96.8	51.0	39.2	66.3

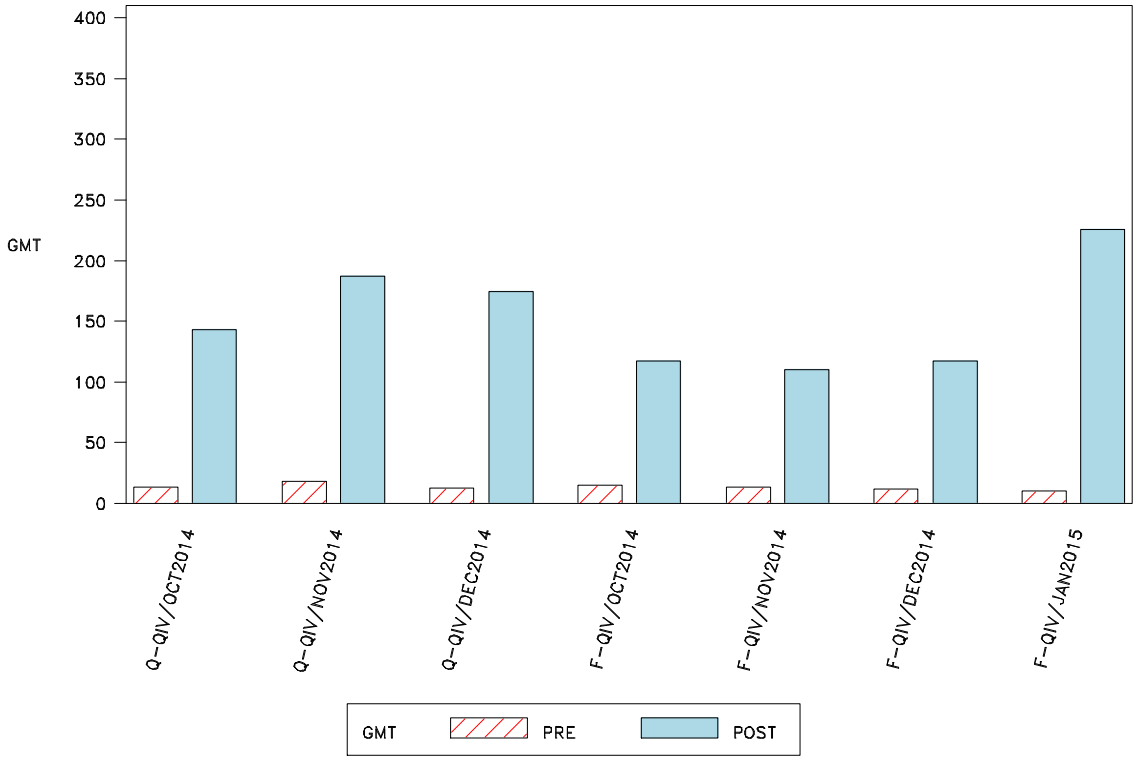
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
*= Time window was classified according to subjects' last dose date
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Figure 5 GMT profiles for Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose by vaccination date (ATP cohort for immunogenicity)



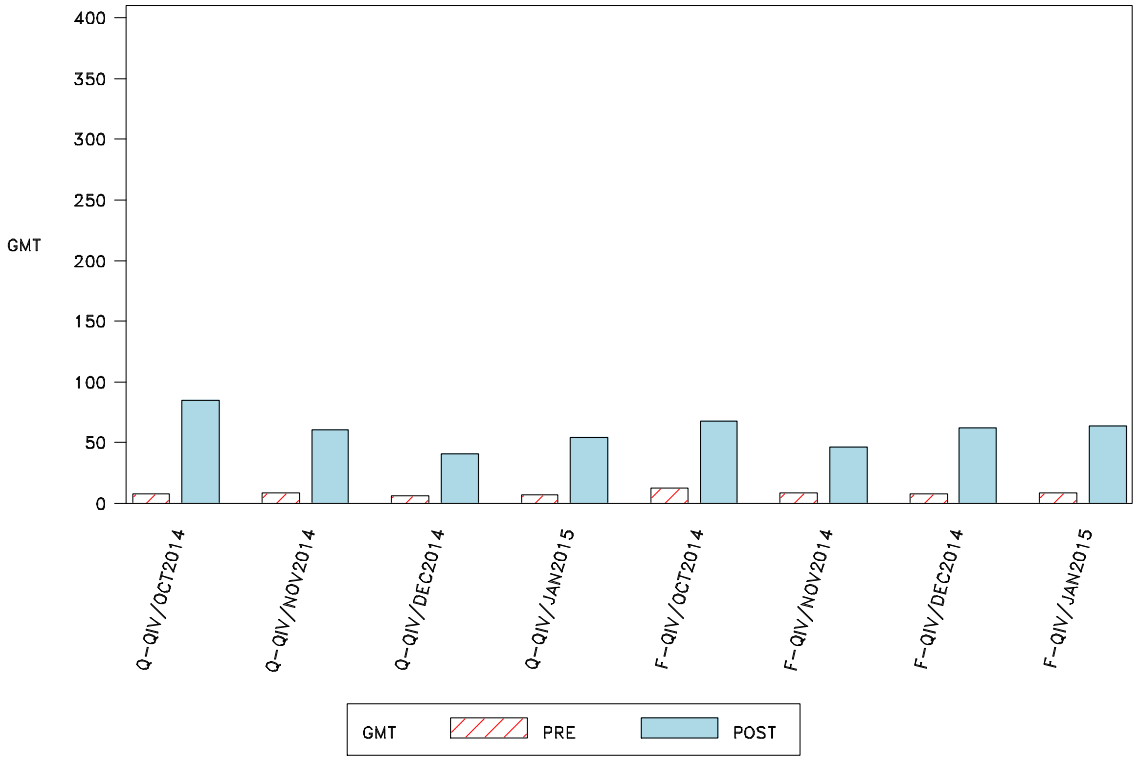
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 6 GMT profiles for Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (ATP cohort for immunogenicity)



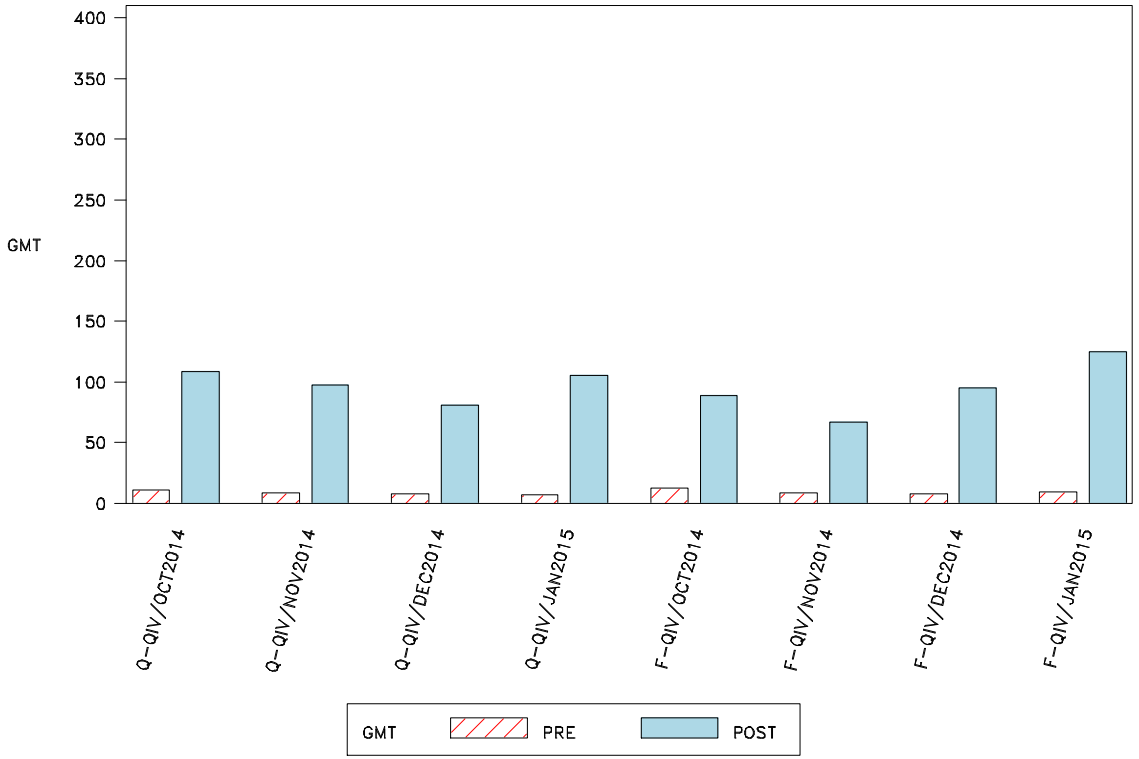
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 7 GMT profiles for Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (ATP cohort for immunogenicity)



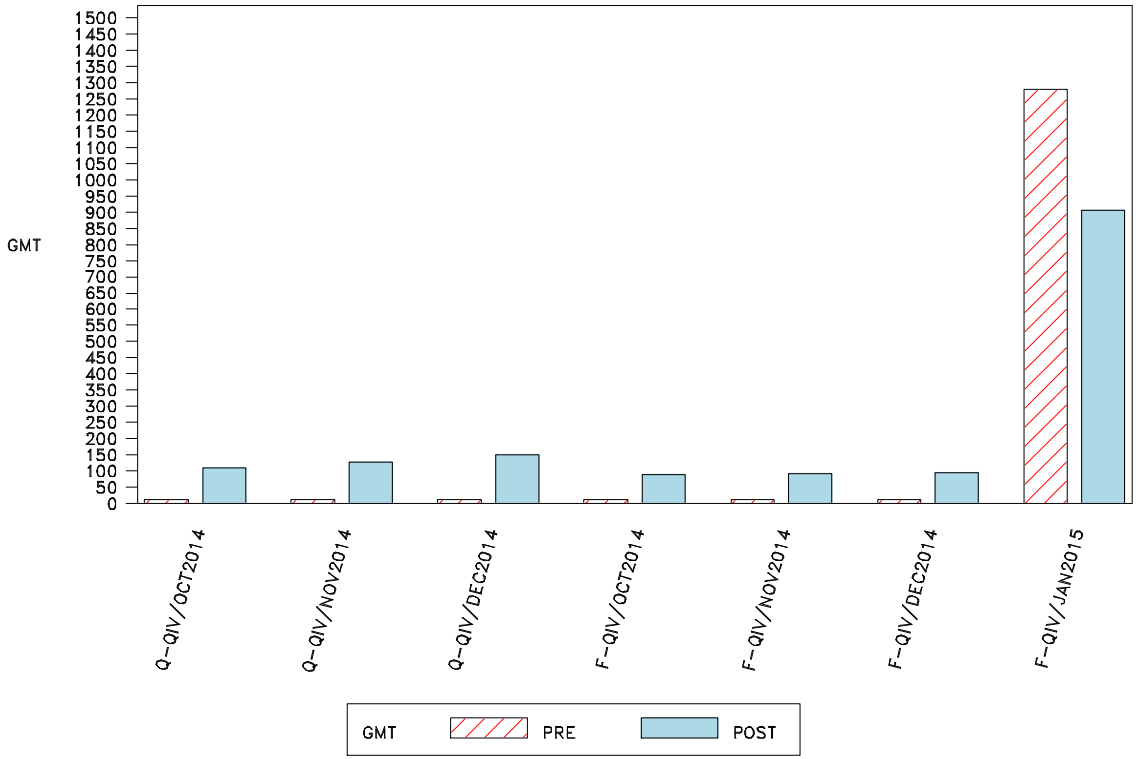
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

Figure 8 GMT profiles for Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose by vaccination date (ATP cohort for immunogenicity)



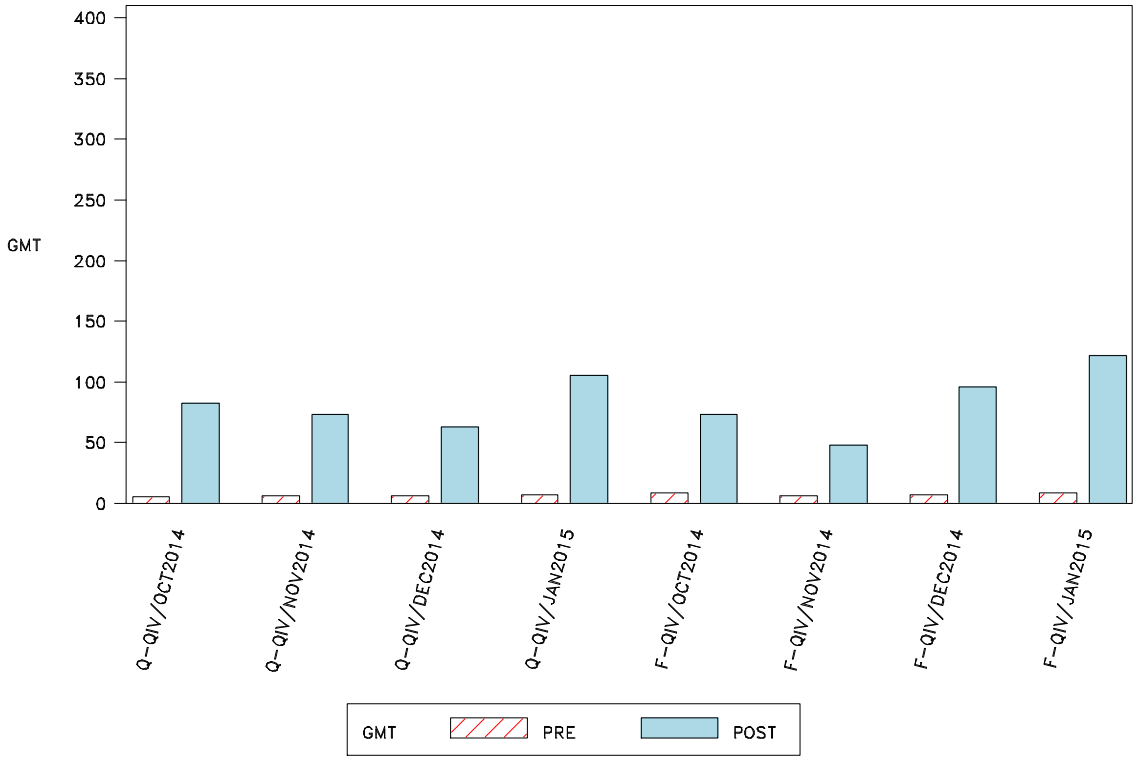
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 9 **GMT profiles for Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (ATP cohort for immunogenicity)**



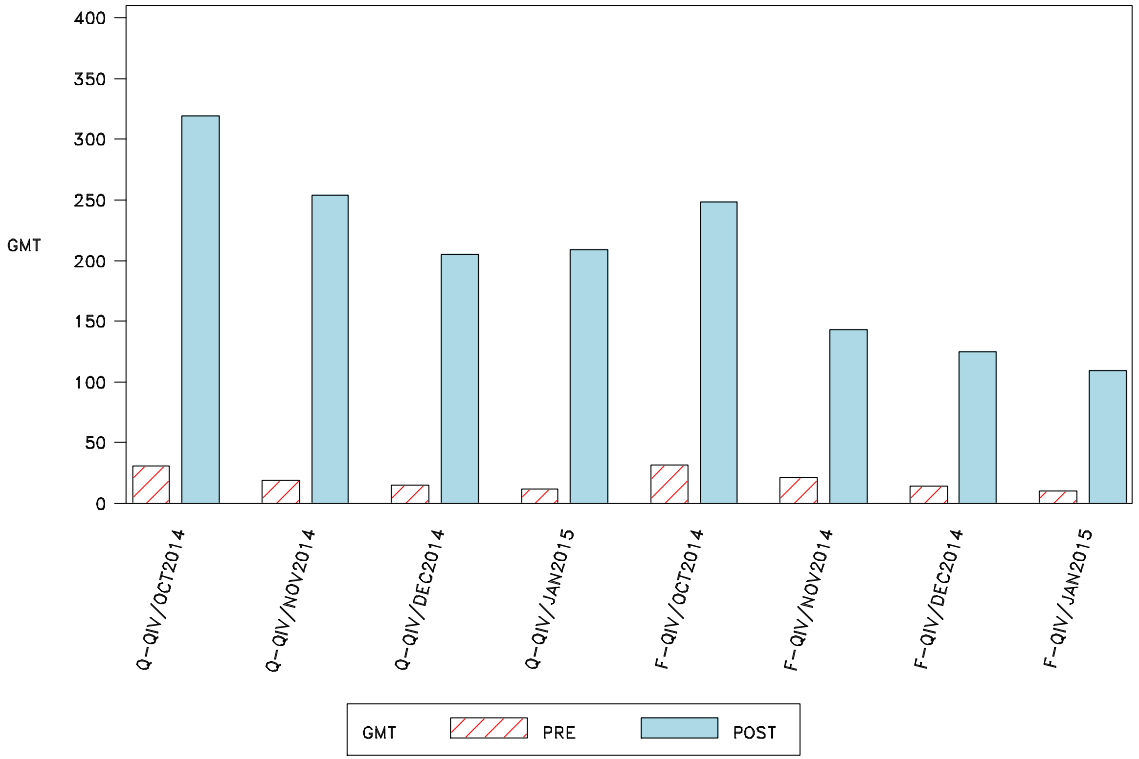
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 10 GMT profiles for Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (ATP cohort for immunogenicity)



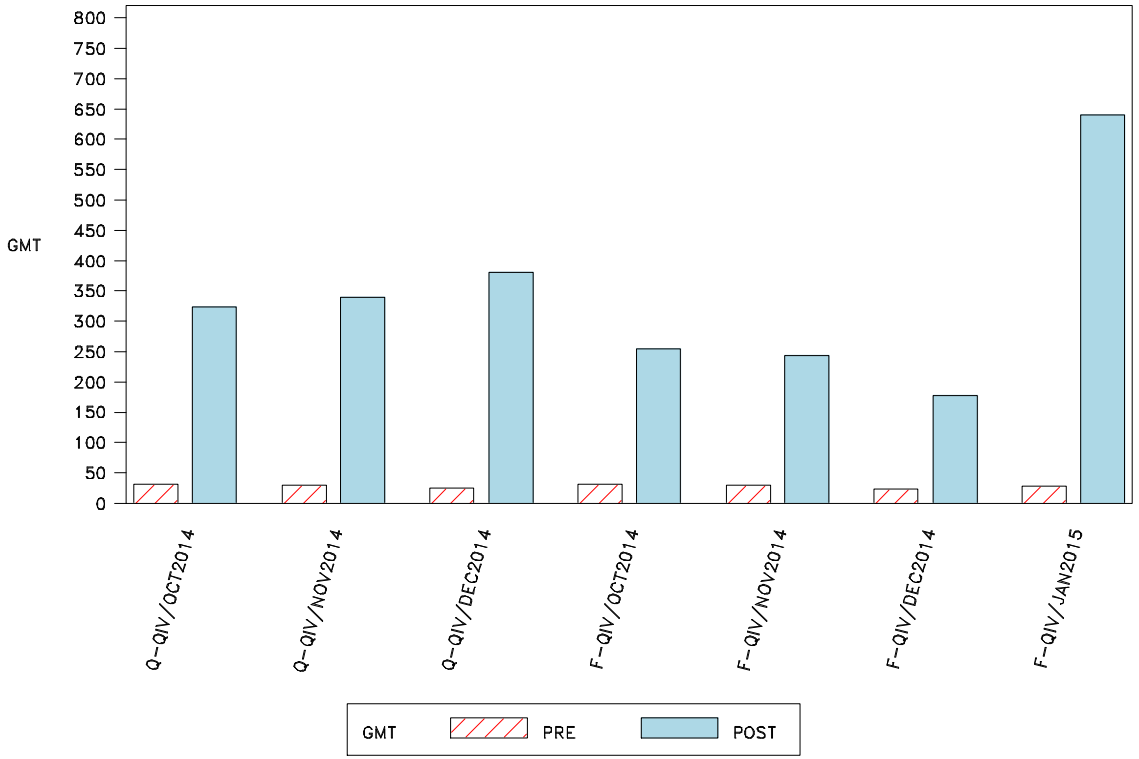
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

Figure 11 GMT profiles for Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose by vaccination date (ATP cohort for immunogenicity)



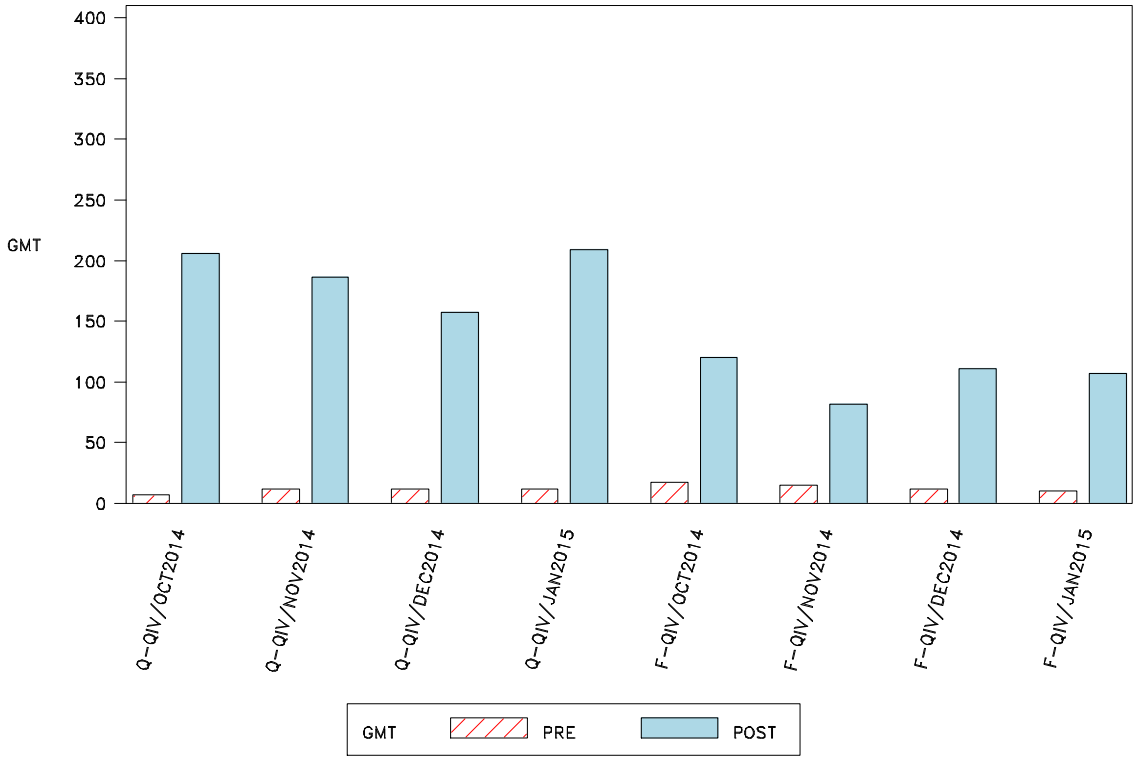
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 12 GMT profiles for Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (ATP cohort for immunogenicity)



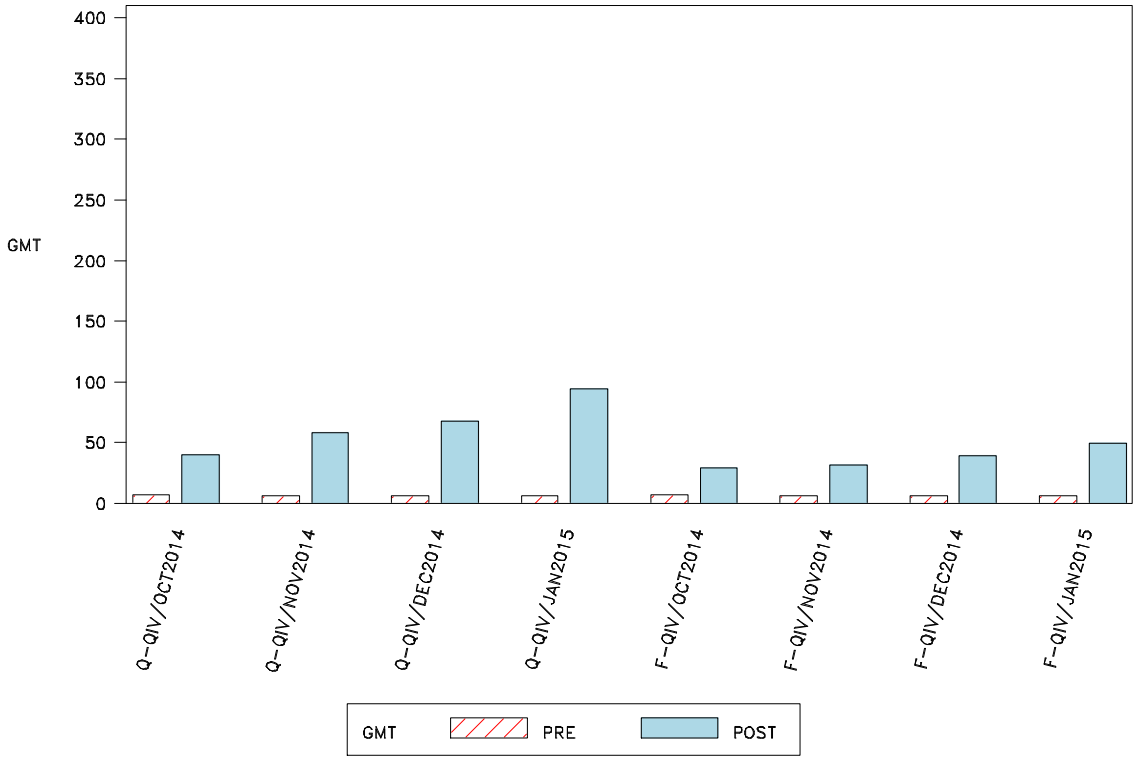
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 13 GMT profiles for Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (ATP cohort for immunogenicity)



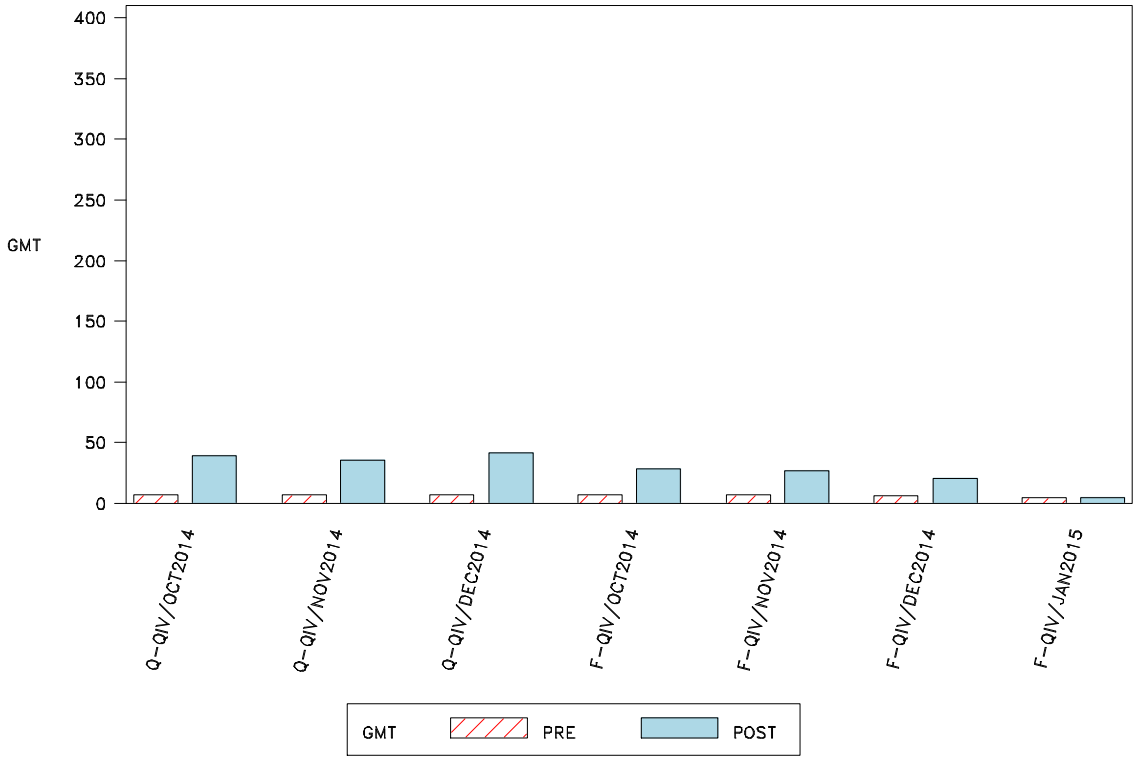
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

Figure 14 GMT profiles for Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose by vaccination date (ATP cohort for immunogenicity)



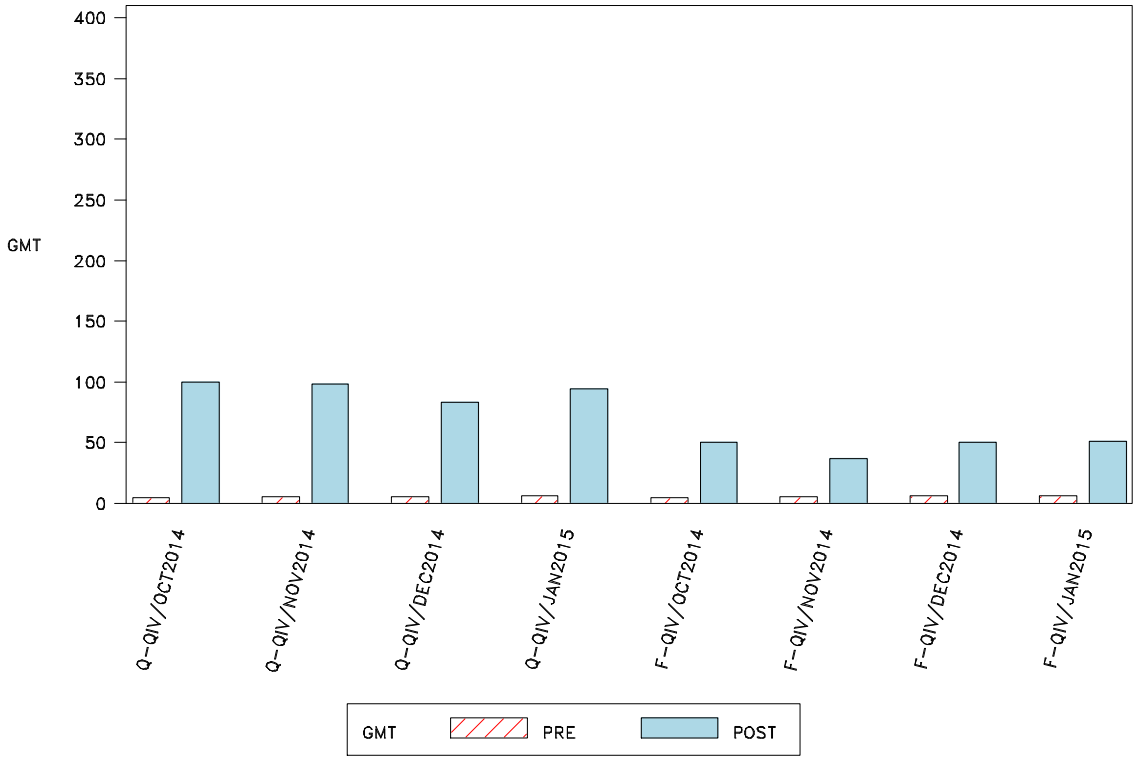
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 15 GMT profiles for Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 16 GMT profiles for Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (ATP cohort for immunogenicity)



Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

Table 79 Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by vaccination date (Total vaccinated cohort)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group*	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	OCT2014	PRE	397	184	46.3	41.4	51.4	12.6	11.2	14.2
			POST	368	363	98.6	96.9	99.6	140.2	123.5	159.2
		NOV2014	PRE	383	147	38.4	33.5	43.5	13.2	11.3	15.3
			POST	361	335	92.8	89.6	95.2	107.4	91.5	126.0
		DEC2014	PRE	249	52	20.9	16.0	26.5	8.2	7.2	9.5
			POST	244	210	86.1	81.1	90.2	61.3	50.4	74.5
		JAN2015	PRE	108	17	15.7	9.4	24.0	7.1	5.9	8.6
			POST	105	100	95.2	89.2	98.4	54.0	42.6	68.4
		FEB2015	PRE	2	1	50.0	1.3	98.7	40.0	0.0	1.194E13
			POST	2	2	100	15.8	100	321.2	0.0	1.117E12
	F-QIV	OCT2014	PRE	396	193	48.7	43.7	53.8	14.7	12.8	16.8
			POST	373	354	94.9	92.2	96.9	117.3	101.9	135.1
		NOV2014	PRE	373	138	37.0	32.1	42.1	10.8	9.5	12.3
			POST	360	312	86.7	82.7	90.0	69.6	58.7	82.4
		DEC2014	PRE	264	67	25.4	20.2	31.1	9.0	7.7	10.4
			POST	255	229	89.8	85.4	93.2	71.4	59.3	86.0
		JAN2015	PRE	106	23	21.7	14.3	30.8	7.9	6.4	9.8
			POST	99	89	89.9	82.2	95.0	64.2	47.5	86.8
		FEB2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	1	100	2.5	100	40.0	-	-
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	OCT2014	PRE	397	186	46.9	41.9	51.9	11.1	9.9	12.4
			POST	368	359	97.6	95.4	98.9	109.4	97.3	122.9
		NOV2014	PRE	383	120	31.3	26.7	36.2	9.0	8.1	9.9
			POST	361	351	97.2	95.0	98.7	96.3	85.0	109.2
		DEC2014	PRE	249	44	17.7	13.1	23.0	7.6	6.6	8.7
			POST	244	234	95.9	92.6	98.0	82.6	69.3	98.4
		JAN2015	PRE	108	14	13.0	7.3	20.8	6.8	5.7	8.0
			POST	105	103	98.1	93.3	99.8	106.6	78.4	145.0
		FEB2015	PRE	2	0	0.0	0.0	84.2	5.0	5.0	5.0
			POST	2	2	100	15.8	100	113.1	1.4	9248.7
	F-QIV	OCT2014	PRE	396	177	44.7	39.7	49.7	11.9	10.5	13.5
			POST	373	361	96.8	94.4	98.3	89.6	79.3	101.2
		NOV2014	PRE	373	104	27.9	23.4	32.7	8.8	7.9	9.9
			POST	360	334	92.8	89.6	95.2	65.8	57.2	75.8
		DEC2014	PRE	264	55	20.8	16.1	26.2	7.8	6.8	8.9
			POST	255	247	96.9	93.9	98.6	94.5	79.3	112.7
		JAN2015	PRE	106	25	23.6	15.9	32.8	8.7	6.8	11.3
			POST	99	94	94.9	88.6	98.3	118.8	87.3	161.8
		FEB2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	1	100	2.5	100	28.0	-	-
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	OCT2014	PRE	398	329	82.7	78.6	86.3	28.9	25.6	32.7
			POST	368	368	100	99.0	100	318.2	285.1	355.1
		NOV2014	PRE	384	260	67.7	62.8	72.4	19.2	16.9	21.8
			POST	361	361	100	99.0	100	250.5	224.4	279.6
		DEC2014	PRE	249	146	58.6	52.2	64.8	13.9	12.1	16.1

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group***	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
			POST	244	244	100	98.5	100	202.6	177.4	231.4
		JAN2015	PRE	108	52	48.1	38.4	58.0	11.3	9.1	13.9
			POST	105	105	100	96.5	100	208.4	170.1	255.2
		FEB2015	PRE	2	2	100	15.8	100	16.7	0.0	11599.0
			POST	2	2	100	15.8	100	452.5	0.0	2.4722E8
	F-QIV	OCT2014	PRE	396	324	81.8	77.7	85.5	29.9	26.3	34.1
			POST	373	371	99.5	98.1	99.9	250.4	221.5	283.1
		NOV2014	PRE	373	267	71.6	66.7	76.1	20.2	17.8	22.9
			POST	360	357	99.2	97.6	99.8	139.5	121.2	160.6
		DEC2014	PRE	264	145	54.9	48.7	61.0	13.7	11.8	15.9
			POST	255	251	98.4	96.0	99.6	122.0	105.4	141.3
		JAN2015	PRE	106	47	44.3	34.7	54.3	9.9	8.2	11.9
			POST	99	99	100	96.3	100	110.7	87.8	139.7
		FEB2015	PRE	1	1	100	2.5	100	14.0	-	-
			POST	1	1	100	2.5	100	80.0	-	-
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	OCT2014	PRE	397	74	18.6	14.9	22.8	6.6	6.2	7.2
			POST	368	330	89.7	86.1	92.6	41.1	35.4	47.7
		NOV2014	PRE	384	43	11.2	8.2	14.8	6.2	5.8	6.7
			POST	361	332	92.0	88.7	94.6	58.0	50.3	66.8
		DEC2014	PRE	249	21	8.4	5.3	12.6	5.8	5.4	6.2
			POST	244	237	97.1	94.2	98.8	69.0	60.5	78.7
		JAN2015	PRE	108	11	10.2	5.2	17.5	5.9	5.3	6.5
			POST	105	104	99.0	94.8	100	94.7	78.1	114.7
		FEB2015	PRE	2	1	50.0	1.3	98.7	23.8	0.0	9.5239E9
			POST	2	2	100	15.8	100	321.2	0.0	1.117E12
	F-QIV	OCT2014	PRE	396	71	17.9	14.3	22.1	6.9	6.3	7.4
			POST	373	280	75.1	70.4	79.4	28.4	24.3	33.2
		NOV2014	PRE	373	47	12.6	9.4	16.4	6.1	5.7	6.6
			POST	360	291	80.8	76.4	84.8	30.7	26.6	35.4
		DEC2014	PRE	264	20	7.6	4.7	11.5	5.8	5.4	6.3
			POST	255	221	86.7	81.9	90.6	39.8	33.9	46.6
		JAN2015	PRE	106	7	6.6	2.7	13.1	6.0	5.2	6.9
			POST	99	91	91.9	84.7	96.4	50.7	39.0	66.0
		FEB2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	1	100	2.5	100	40.0	-	-

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
*= Time window was classified according to subjects' last dose date
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Table 80 Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by vaccination date for primed subjects (Total vaccinated cohort)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group*	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	OCT2014	PRE	375	182	48.5	43.4	53.7	13.1	11.6	14.9
			POST	354	349	98.6	96.7	99.5	145.1	127.7	164.8
		NOV2014	PRE	190	97	51.1	43.7	58.4	16.8	13.5	20.8
			POST	185	180	97.3	93.8	99.1	176.7	144.8	215.7
		DEC2014	PRE	70	28	40.0	28.5	52.4	12.6	9.0	17.4
			POST	68	66	97.1	89.8	99.6	174.5	128.8	236.3
	F-QIV	OCT2014	PRE	370	188	50.8	45.6	56.0	15.2	13.2	17.5
			POST	361	345	95.6	92.9	97.4	119.5	103.8	137.5
		NOV2014	PRE	187	92	49.2	41.8	56.6	13.4	11.1	16.2
			POST	184	171	92.9	88.2	96.2	108.7	87.5	135.1
		DEC2014	PRE	68	28	41.2	29.4	53.8	11.9	8.6	16.4
			POST	64	59	92.2	82.7	97.4	111.8	76.2	164.1
		JAN2015	PRE	1	1	100	2.5	100	10.0	-	-
			POST	1	1	100	2.5	100	226.0	-	-
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	OCT2014	PRE	375	184	49.1	43.9	54.2	11.6	10.3	13.0
			POST	354	345	97.5	95.2	98.8	111.5	99.1	125.4
		NOV2014	PRE	190	90	47.4	40.1	54.7	12.0	10.2	14.1
			POST	185	181	97.8	94.6	99.4	125.4	104.6	150.3
		DEC2014	PRE	70	27	38.6	27.2	51.0	11.9	8.4	16.9
			POST	68	68	100	94.7	100	149.6	112.0	199.8
	F-QIV	OCT2014	PRE	370	173	46.8	41.6	52.0	12.4	10.9	14.1
			POST	361	350	97.0	94.6	98.5	90.2	79.6	102.1
		NOV2014	PRE	187	86	46.0	38.7	53.4	12.5	10.4	15.1
			POST	184	180	97.8	94.5	99.4	91.1	75.5	109.8
		DEC2014	PRE	68	27	39.7	28.0	52.3	10.5	7.7	14.4
			POST	64	63	98.4	91.6	100	94.1	67.8	130.7
		JAN2015	PRE	1	1	100	2.5	100	1280.0	-	-
			POST	1	1	100	2.5	100	905.0	-	-
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	OCT2014	PRE	376	322	85.6	81.7	89.0	31.3	27.6	35.5
			POST	354	354	100	99.0	100	325.4	291.2	363.5
		NOV2014	PRE	191	153	80.1	73.7	85.5	28.2	23.4	33.9
			POST	185	185	100	98.0	100	332.2	282.7	390.3
		DEC2014	PRE	70	60	85.7	75.3	92.9	24.8	18.8	32.8
			POST	68	68	100	94.7	100	380.6	294.8	491.3
	F-QIV	OCT2014	PRE	370	308	83.2	79.0	86.9	31.6	27.7	36.2
			POST	361	359	99.4	98.0	99.9	256.6	226.4	290.9
		NOV2014	PRE	187	154	82.4	76.1	87.5	29.1	24.2	35.0
			POST	184	181	98.4	95.3	99.7	238.5	197.1	288.5
		DEC2014	PRE	68	50	73.5	61.4	83.5	23.5	16.8	32.9
			POST	64	63	98.4	91.6	100	173.4	125.6	239.5
		JAN2015	PRE	1	1	100	2.5	100	28.0	-	-
			POST	1	1	100	2.5	100	640.0	-	-

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group***	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	OCT2014	PRE	375	74	19.7	15.8	24.1	6.8	6.3	7.3
			POST	354	316	89.3	85.6	92.3	40.1	34.5	46.7
		NOV2014	PRE	191	28	14.7	10.0	20.5	6.6	5.9	7.4
			POST	185	159	85.9	80.1	90.6	34.9	28.2	43.1
		DEC2014	PRE	70	12	17.1	9.2	28.0	6.8	5.7	8.0
			POST	68	61	89.7	79.9	95.8	41.4	29.5	58.3
	F-QIV	OCT2014	PRE	370	69	18.6	14.8	23.0	6.9	6.4	7.6
			POST	361	269	74.5	69.7	78.9	27.8	23.7	32.7
		NOV2014	PRE	187	35	18.7	13.4	25.1	7.0	6.2	8.0
			POST	184	133	72.3	65.2	78.6	26.9	21.4	33.8
		DEC2014	PRE	68	5	7.4	2.4	16.3	6.1	5.0	7.4
			POST	64	41	64.1	51.1	75.7	19.5	13.8	27.5
		JAN2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	0	0.0	0.0	97.5	5.0	-	-

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
*= Time window was classified according to subjects' last dose date
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

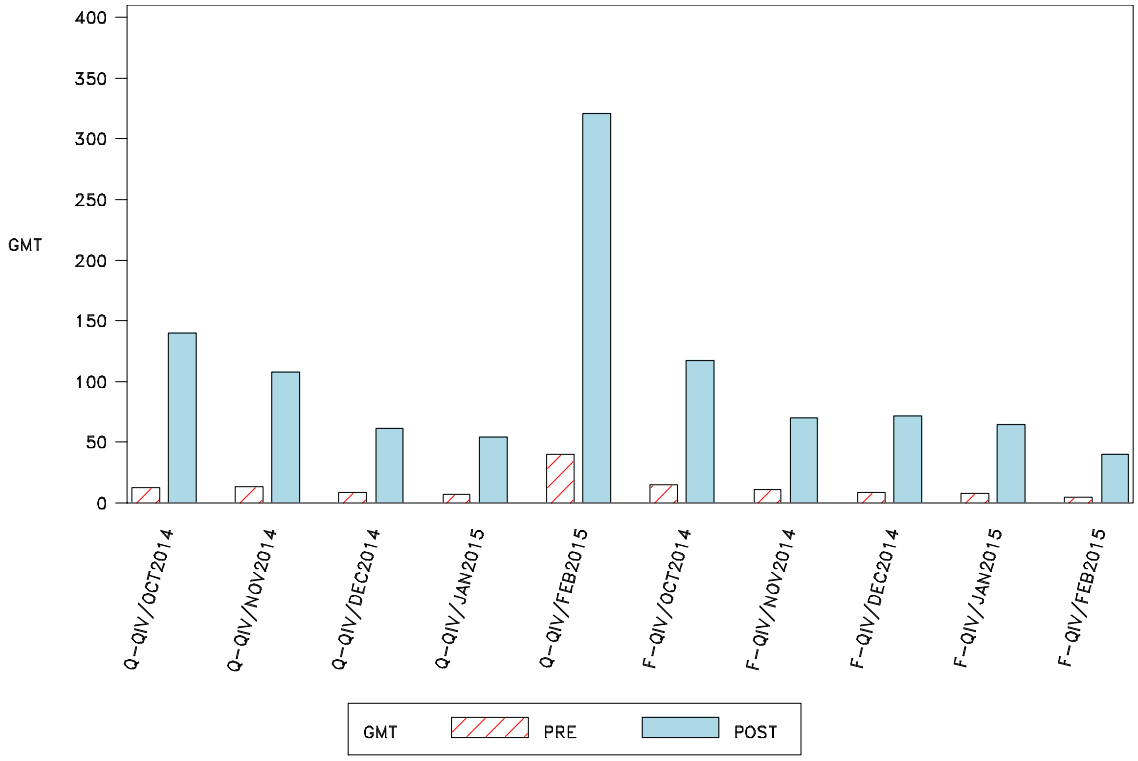
Table 81 Seropositivity rates and GMTs for HI antibodies against A/California/7/2009 (H1N1), A/Texas/50/2012 (H3N2), B/Massachusetts/2/2012 (Yamagata), B/Brisbane/60/2008 (Victoria) at Day 0 and 28 days after the last vaccine dose by vaccination date for unprimed subjects (Total vaccinated cohort)

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	Group	Sub-group*	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/California/7/2009 H1N1 HI (1/DIL)	Q-QIV	OCT2014	PRE	22	2	9.1	1.1	29.2	6.2	4.5	8.7
			POST	14	14	100	76.8	100	59.3	25.8	136.2
		NOV2014	PRE	193	50	25.9	19.9	32.7	10.4	8.5	12.7
			POST	176	155	88.1	82.3	92.5	63.6	50.6	80.1
		DEC2014	PRE	179	24	13.4	8.8	19.3	7.0	6.0	8.1
			POST	176	144	81.8	75.3	87.2	40.9	32.9	50.9
		JAN2015	PRE	108	17	15.7	9.4	24.0	7.1	5.9	8.6
			POST	105	100	95.2	89.2	98.4	54.0	42.6	68.4
		FEB2015	PRE	2	1	50.0	1.3	98.7	40.0	0.0	1.194E13
			POST	2	2	100	15.8	100	321.2	0.0	1.117E12
	F-QIV	OCT2014	PRE	26	5	19.2	6.6	39.4	8.5	5.1	14.2
			POST	12	9	75.0	42.8	94.5	67.3	17.7	255.1
		NOV2014	PRE	186	46	24.7	18.7	31.6	8.7	7.4	10.4
			POST	176	141	80.1	73.4	85.7	43.6	34.1	55.7
		DEC2014	PRE	196	39	19.9	14.5	26.2	8.1	6.9	9.6
			POST	191	170	89.0	83.7	93.1	61.5	49.9	75.8
		JAN2015	PRE	105	22	21.0	13.6	30.0	7.9	6.3	9.8
			POST	98	88	89.8	82.0	95.0	63.4	46.8	85.8
		FEB2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	1	100	2.5	100	40.0	-	-
Flu A/Texas/50/2012 H3N2 HI (1/DIL)	Q-QIV	OCT2014	PRE	22	2	9.1	1.1	29.2	5.3	4.9	5.8
			POST	14	14	100	76.8	100	67.2	29.4	153.5
		NOV2014	PRE	193	30	15.5	10.7	21.4	6.7	6.0	7.6
			POST	176	170	96.6	92.7	98.7	73.1	62.0	86.1
		DEC2014	PRE	179	17	9.5	5.6	14.8	6.4	5.6	7.2
			POST	176	166	94.3	89.8	97.2	65.7	53.3	80.8
		JAN2015	PRE	108	14	13.0	7.3	20.8	6.8	5.7	8.0
			POST	105	103	98.1	93.3	99.8	106.6	78.4	145.0
		FEB2015	PRE	2	0	0.0	0.0	84.2	5.0	5.0	5.0
			POST	2	2	100	15.8	100	113.1	1.4	9248.7
	F-QIV	OCT2014	PRE	26	4	15.4	4.4	34.9	6.6	4.8	9.2
			POST	12	11	91.7	61.5	99.8	73.4	35.0	153.7
		NOV2014	PRE	186	18	9.7	5.8	14.9	6.2	5.5	6.9
			POST	176	154	87.5	81.7	92.0	46.9	38.4	57.4
		DEC2014	PRE	196	28	14.3	9.7	20.0	7.0	6.1	8.0
			POST	191	184	96.3	92.6	98.5	94.7	76.9	116.6
		JAN2015	PRE	105	24	22.9	15.2	32.1	8.3	6.6	10.6
			POST	98	93	94.9	88.5	98.3	116.4	85.4	158.5
		FEB2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	1	100	2.5	100	28.0	-	-
Flu B/Massachusetts/2/2012 Yamagata HI (1/DIL)	Q-QIV	OCT2014	PRE	22	7	31.8	13.9	54.9	7.4	5.5	10.0
			POST	14	14	100	76.8	100	180.9	89.8	364.7
		NOV2014	PRE	193	107	55.4	48.1	62.6	13.1	11.3	15.3
			POST	176	176	100	97.9	100	186.2	162.3	213.6

					≥ 10 1/DIL				GMT		
							95% CI			95% CI	
Antibody	**Group**	**Sub-group***	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
		DEC2014	PRE	179	86	48.0	40.5	55.6	11.1	9.5	13.0
			POST	176	176	100	97.9	100	158.8	137.9	182.9
		JAN2015	PRE	108	52	48.1	38.4	58.0	11.3	9.1	13.9
			POST	105	105	100	96.5	100	208.4	170.1	255.2
		FEB2015	PRE	2	2	100	15.8	100	16.7	0.0	11599.0
			POST	2	2	100	15.8	100	452.5	0.0	2.4722E8
	F-QIV	OCT2014	PRE	26	16	61.5	40.6	79.8	13.6	8.7	21.2
			POST	12	12	100	73.5	100	119.9	76.6	187.7
		NOV2014	PRE	186	113	60.8	53.3	67.8	14.0	12.0	16.3
			POST	176	176	100	97.9	100	79.6	66.9	94.8
		DEC2014	PRE	196	95	48.5	41.3	55.7	11.4	9.8	13.3
			POST	191	188	98.4	95.5	99.7	108.5	92.4	127.4
		JAN2015	PRE	105	46	43.8	34.1	53.8	9.8	8.2	11.7
			POST	98	98	100	96.3	100	108.8	86.3	137.1
		FEB2015	PRE	1	1	100	2.5	100	14.0	-	-
			POST	1	1	100	2.5	100	80.0	-	-
Flu B/Brisbane/60/2008 Victoria HI (1/DIL)	Q-QIV	OCT2014	PRE	22	0	0.0	0.0	15.4	5.0	5.0	5.0
			POST	14	14	100	76.8	100	76.1	38.9	148.8
		NOV2014	PRE	193	15	7.8	4.4	12.5	5.8	5.3	6.4
			POST	176	173	98.3	95.1	99.6	99.0	84.6	115.7
		DEC2014	PRE	179	9	5.0	2.3	9.3	5.4	5.1	5.8
			POST	176	176	100	97.9	100	84.0	74.7	94.5
		JAN2015	PRE	108	11	10.2	5.2	17.5	5.9	5.3	6.5
			POST	105	104	99.0	94.8	100	94.7	78.1	114.7
		FEB2015	PRE	2	1	50.0	1.3	98.7	23.8	0.0	9.5239E9
			POST	2	2	100	15.8	100	321.2	0.0	1.117E12
	F-QIV	OCT2014	PRE	26	2	7.7	0.9	25.1	5.9	4.6	7.5
			POST	12	11	91.7	61.5	99.8	50.4	25.5	99.4
		NOV2014	PRE	186	12	6.5	3.4	11.0	5.4	5.1	5.7
			POST	176	158	89.8	84.3	93.8	35.2	29.7	41.7
		DEC2014	PRE	196	15	7.7	4.3	12.3	5.8	5.3	6.3
			POST	191	180	94.2	89.9	97.1	50.5	42.8	59.7
		JAN2015	PRE	105	7	6.7	2.7	13.3	6.0	5.2	6.9
			POST	98	91	92.9	85.8	97.1	52.0	40.0	67.5
		FEB2015	PRE	1	0	0.0	0.0	97.5	5.0	-	-
			POST	1	1	100	2.5	100	40.0	-	-

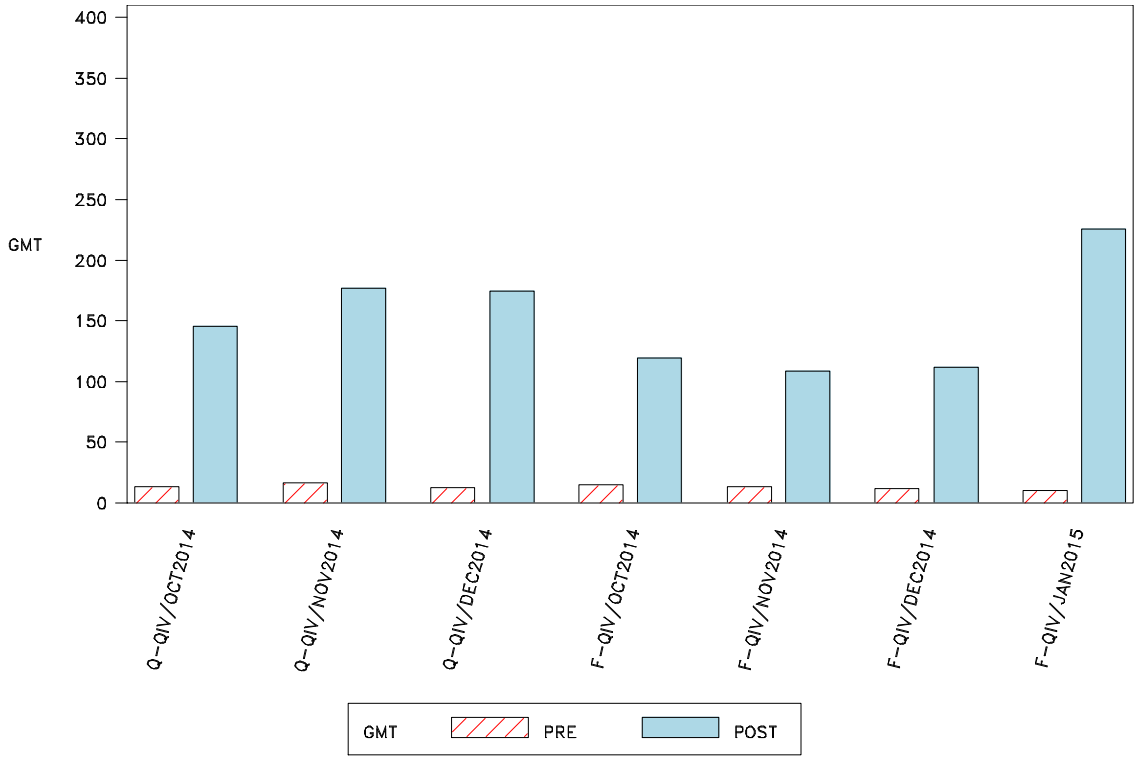
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
*= Time window was classified according to subjects' last dose date
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects.

Figure 17 GMT profiles for Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose by vaccination date (Total vaccinated cohort)



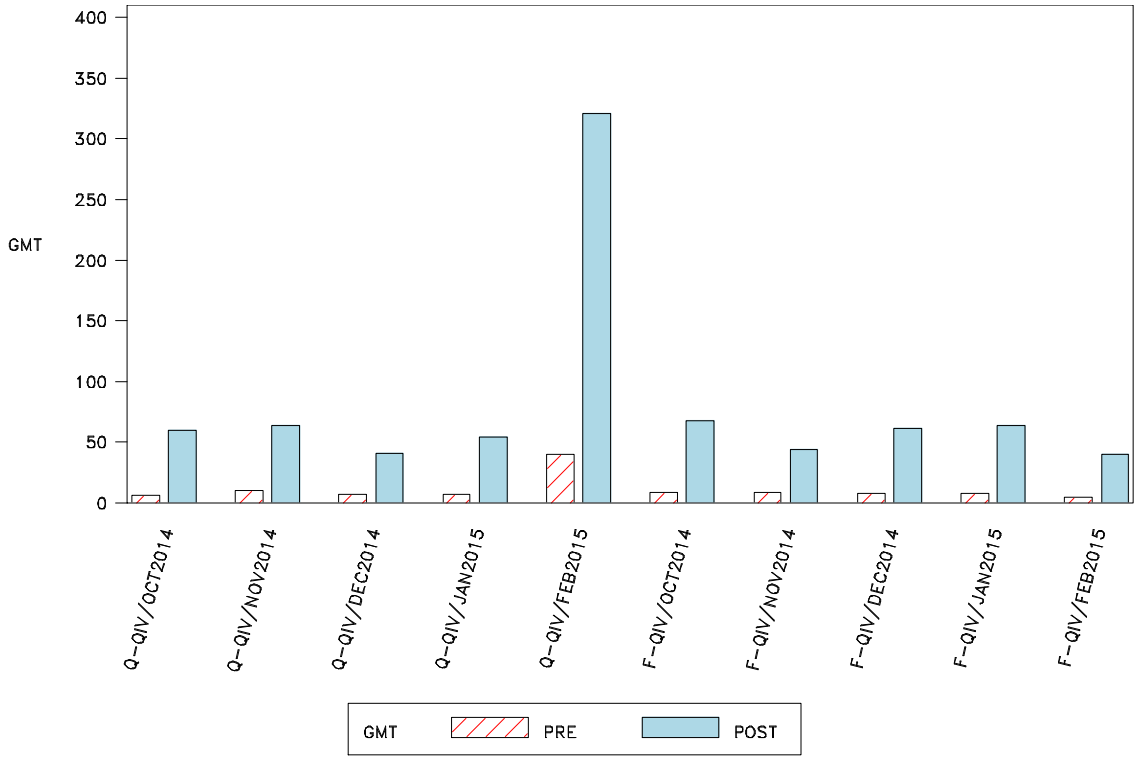
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 18 GMT profiles for Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (Total vaccinated cohort)



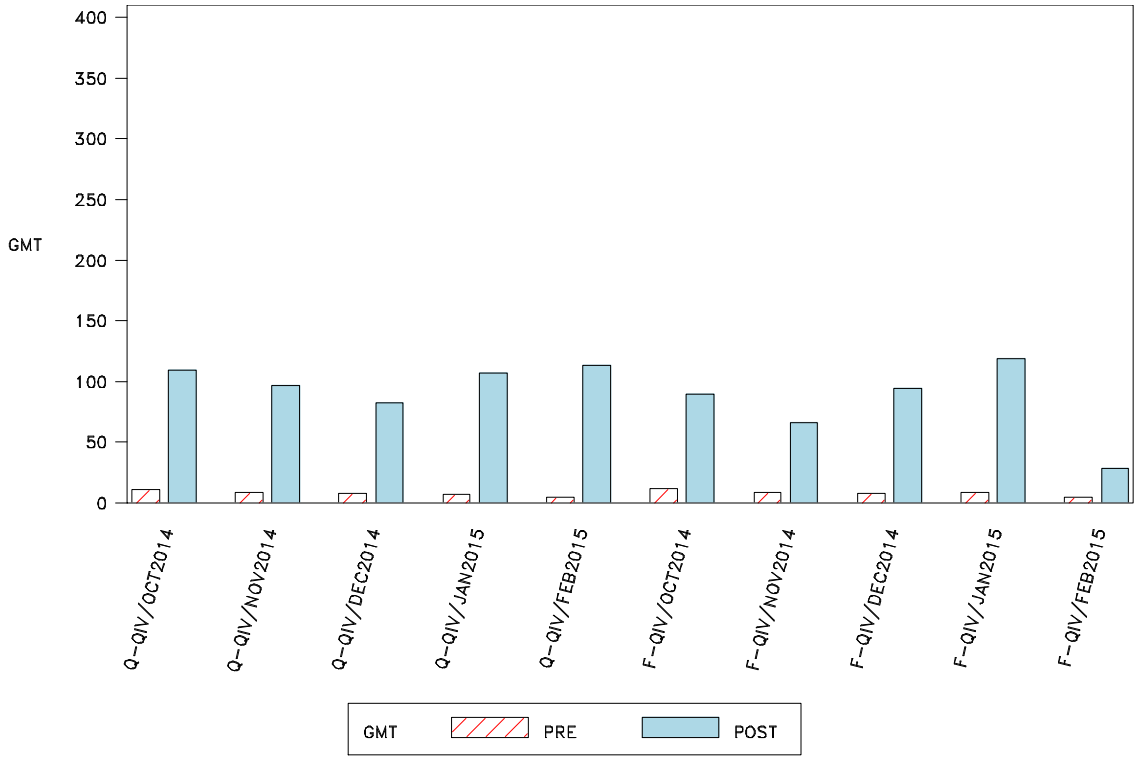
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 19 GMT profiles for Flu A/California/7/2009 (H1N1) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (Total vaccinated cohort)



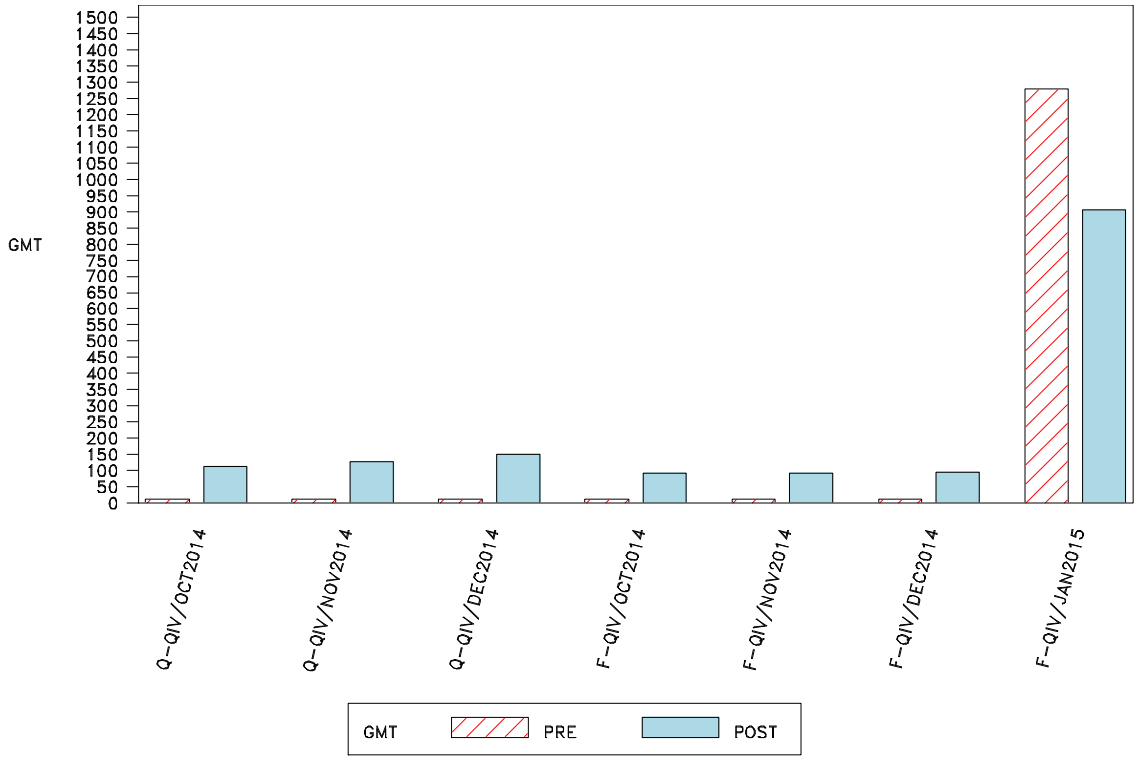
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

Figure 20 GMT profiles for Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose by vaccination date (Total vaccinated cohort)



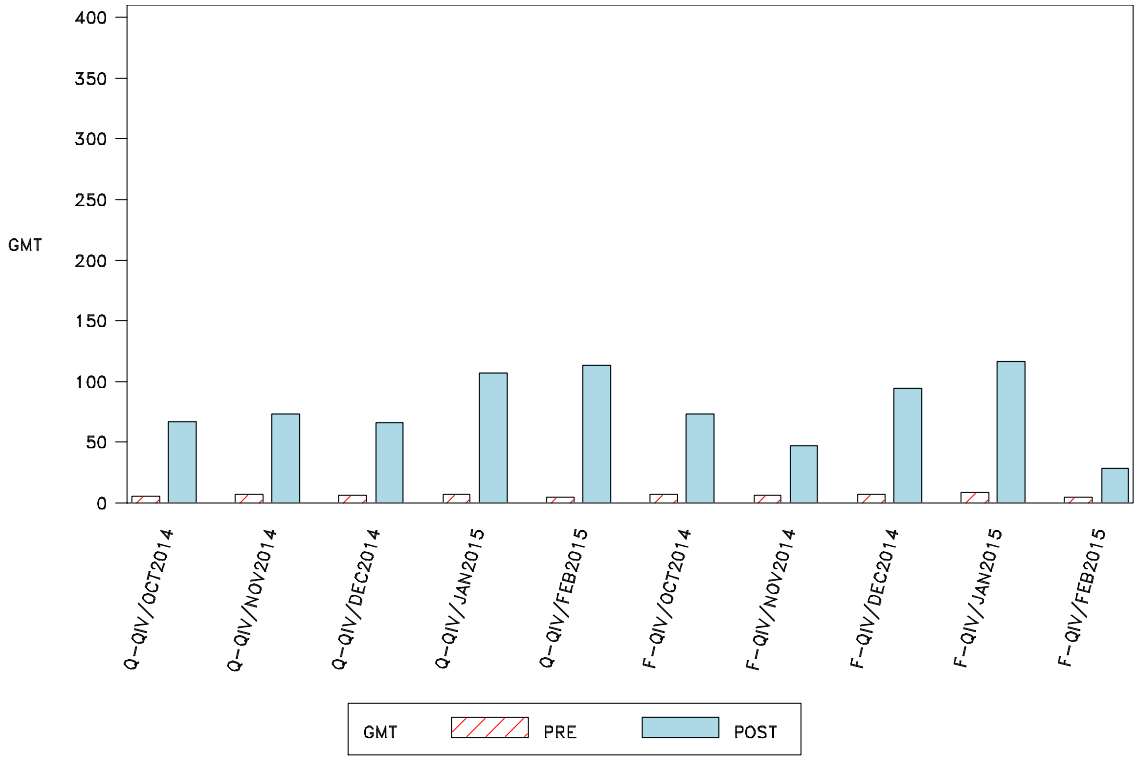
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 21 GMT profiles for Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (Total vaccinated cohort)



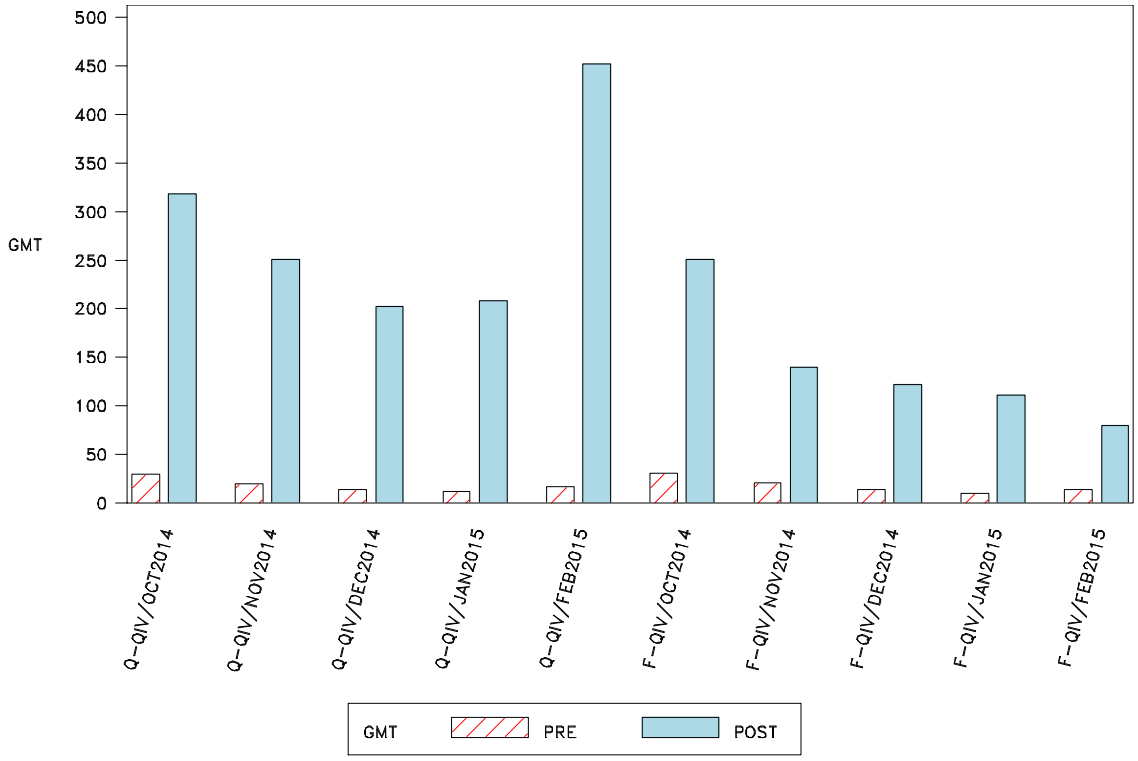
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 22 GMT profiles for Flu A/Texas/50/2012 (H3N2) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (Total vaccinated cohort)



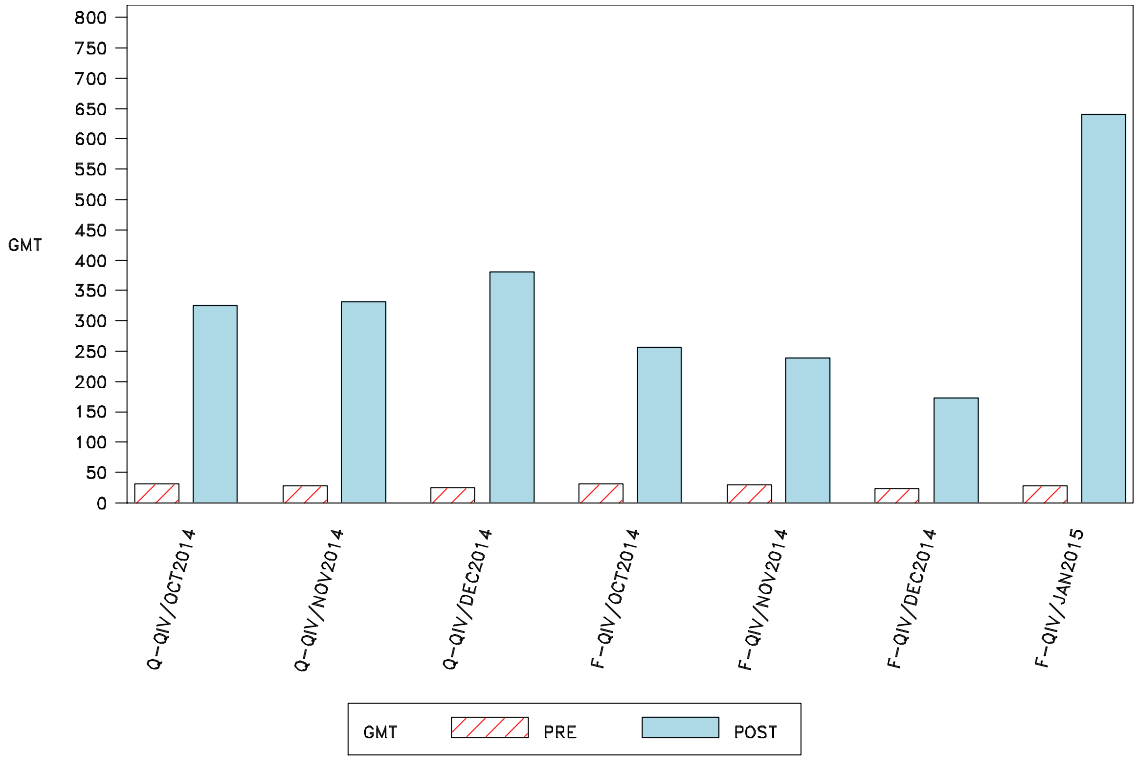
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

Figure 23 GMT profiles for Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose by vaccination date (Total vaccinated cohort)



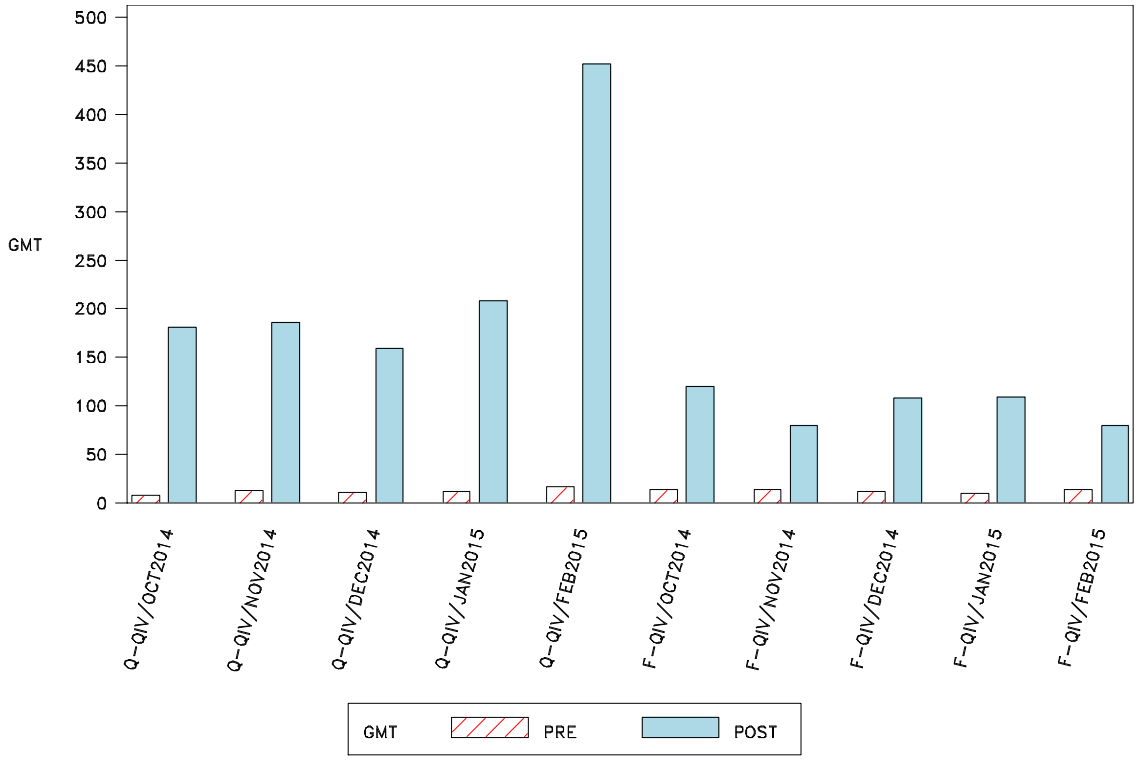
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 24 GMT profiles for Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (Total vaccinated cohort)



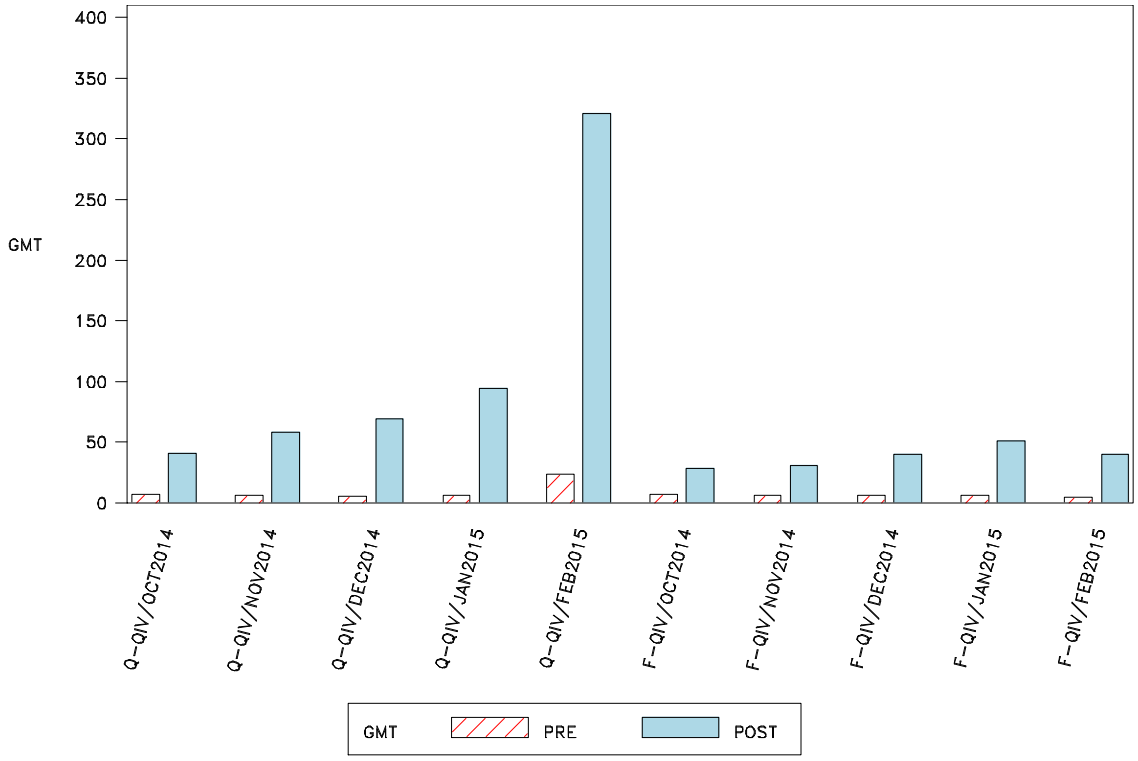
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 25 GMT profiles for Flu B/Massachusetts/2/2012 (Yamagata) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (Total vaccinated cohort)



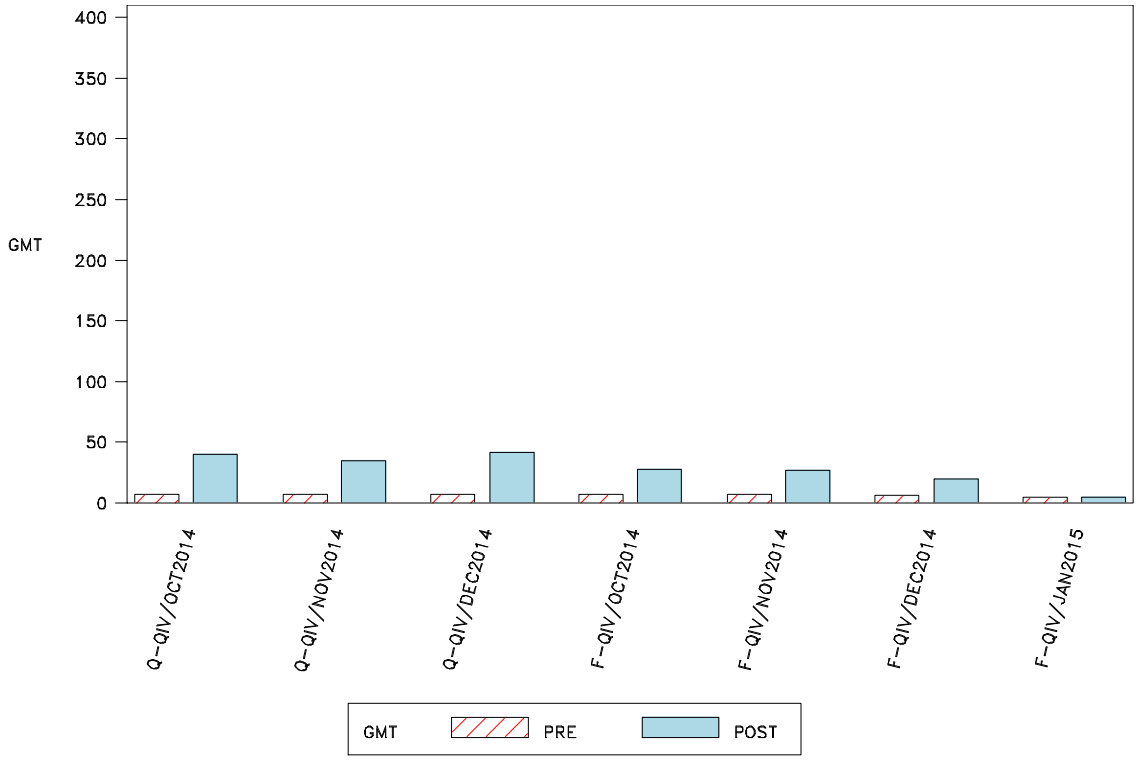
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

Figure 26 GMT profiles for Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose by vaccination date (Total vaccinated cohort)



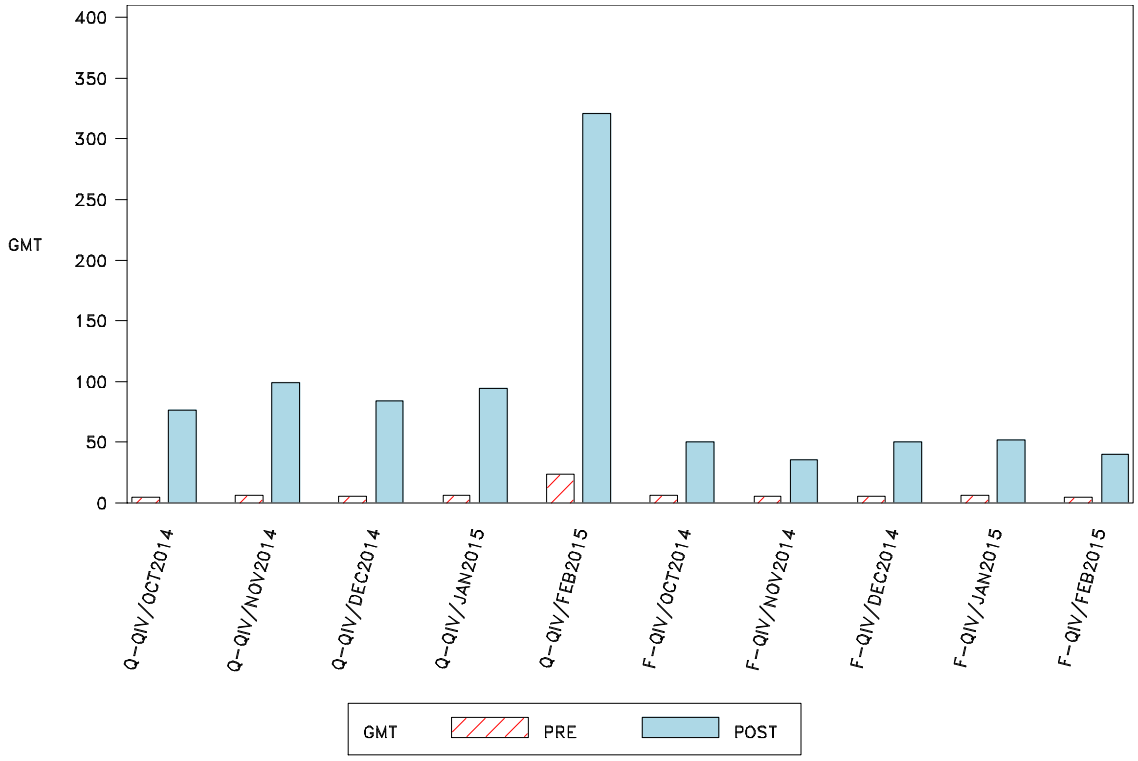
Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects and Visit 3 at Day 56 for unprimed subjects

Figure 27 GMT profiles for Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose by vaccination date for primed subjects (Total vaccinated cohort)



Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 2 at Day 28 for primed subjects

Figure 28 GMT profiles for Flu B/Brisbane/60/2008 (Victoria) HI antibodies at Day 0 and 28 days after last dose by vaccination date for unprimed subjects (Total vaccinated cohort)



Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
Time window was classified according to subjects last dose date GMT = geometric mean antibody titre calculated on all subjects
PRE = Visit Day 0
POST = Visit 3 at Day 56 for unprimed subjects

10.3. Safety

10.3.1. TVC for Safety

Table 82 Compliance in returning symptom sheets (Total vaccinated cohort)

Dose	Group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
1	Q-QIV	1207	215	1155	95.7	1151	95.4
	F-QIV	1217	216	1148	94.3	1146	94.2
2	Q-QIV	519	63	490	94.4	490	94.4
	F-QIV	529	49	495	93.6	493	93.2
Total	Q-QIV	1726	278	1645	95.3	1641	95.1
	F-QIV	1746	265	1643	94.1	1639	93.9

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Table 83 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		549	45.5	42.6	48.3	537	44.1	41.3	47.0
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Iron deficiency anaemia (10022972)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Leukocytosis (10024378)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Lymphadenopathy (10025197)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Neutropenia (10029354)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Congenital, familial and genetic disorders (10010331)	Phimosis (10034878)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Tibial torsion (10064515)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	2	0.2	0.0	0.6	5	0.4	0.1	1.0
	Ear discomfort (10052137)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Ear pain (10014020)	6	0.5	0.2	1.1	2	0.2	0.0	0.6
	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Middle ear effusion (10062545)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dacryostenosis acquired (10053990)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Eye discharge (10015915)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Eye pruritus (10052140)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Eyelid oedema (10015993)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Lacrimation increased (10023644)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Photophobia (10034960)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Gastrointestinal disorders (10017947)	Abdominal discomfort (10000059)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Abdominal hernia (10060954)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Abdominal pain upper (10000087)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Constipation (10010774)	5	0.4	0.1	1.0	5	0.4	0.1	1.0
	Dental caries (10012318)	3	0.2	0.1	0.7	0	0.0	0.0	0.3
	Diarrhoea (10012735)	66	5.5	4.3	6.9	53	4.4	3.3	5.7
	Faeces hard (10016101)	0	0.0	0.0	0.3	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Flatulence (10016766)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Food poisoning (10016952)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Frequent bowel movements (10017367)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Haematochezia (10018836)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Intussusception (10022863)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Nausea (10028813)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Regurgitation (10067171)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Stomatitis (10042128)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Teething (10043183)	15	1.2	0.7	2.0	21	1.7	1.1	2.6
	Vomiting (10047700)	47	3.9	2.9	5.1	46	3.8	2.8	5.0
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Administration site rash (10071156)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Asthenia (10003549)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Chills (10008531)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Developmental delay (10012559)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Discomfort (10013082)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Fatigue (10016256)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Feeling hot (10016334)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Ill-defined disorder (10061520)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Influenza like illness (10022004)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Injection site bruising (10022052)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Injection site pruritus (10022093)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Injection site rash (10022094)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Injection site warmth (10022112)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Local swelling (10024770)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Malaise (10025482)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Pain (10033371)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Pyrexia (10037660)	54	4.5	3.4	5.8	56	4.6	3.5	5.9
	Thirst (10043458)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Vaccination site pain (10068879)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.3	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Vaccination site rash (10069482)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Vaccination site reaction (10059080)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Vaccination site swelling (10069620)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Vessel puncture site haemorrhage (10054092)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Immune system disorders (10021428)	Drug hypersensitivity (10013700)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Hypersensitivity (10020751)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Multiple allergies (10028164)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Seasonal allergy (10048908)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Acarodermatitis (10063409)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Acute sinusitis (10001076)	1	0.1	0.0	0.5	5	0.4	0.1	1.0
	Bronchiolitis (10006448)	9	0.7	0.3	1.4	16	1.3	0.8	2.1
	Bronchitis (10006451)	3	0.2	0.1	0.7	9	0.7	0.3	1.4
	Candida infection (10074170)	0	0.0	0.0	0.3	3	0.2	0.1	0.7
	Candida nappy rash (10007135)	4	0.3	0.1	0.8	1	0.1	0.0	0.5
	Cellulitis (10007882)	2	0.2	0.0	0.6	3	0.2	0.1	0.7
	Clostridium difficile infection (10054236)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Conjunctivitis (10010741)	13	1.1	0.6	1.8	20	1.6	1.0	2.5
	Conjunctivitis bacterial (10061784)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Coxsackie viral infection (10011261)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Croup infectious (10011416)	15	1.2	0.7	2.0	14	1.2	0.6	1.9
	Dermatophytosis (10012504)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Ear infection (10014011)	10	0.8	0.4	1.5	11	0.9	0.5	1.6
	Enterobiasis (10014881)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Exanthema subitum (10015586)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Eye infection (10015929)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Folliculitis (10016936)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Fungal infection (10017533)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Fungal skin infection (10017543)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Gastroenteritis (10017888)	14	1.2	0.6	1.9	22	1.8	1.1	2.7
	Gastroenteritis viral (10017918)	4	0.3	0.1	0.8	4	0.3	0.1	0.8
	Genital candidiasis (10018143)	0	0.0	0.0	0.3	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
	Groin abscess (10050269)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Hand-foot-and-mouth disease (10019113)	7	0.6	0.2	1.2	6	0.5	0.2	1.1
	Herpangina (10019936)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Impetigo (10021531)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Influenza (10022000)	7	0.6	0.2	1.2	7	0.6	0.2	1.2
	Lice infestation (10024424)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Localised infection (10024774)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Lower respiratory tract infection (10024968)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Molluscum contagiosum (10027807)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Nasopharyngitis (10028810)	66	5.5	4.3	6.9	54	4.4	3.4	5.8
	Neonatal candida infection (10028924)	3	0.2	0.1	0.7	0	0.0	0.0	0.3
	Oral candidiasis (10030963)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Otitis externa (10033072)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Otitis media (10033078)	61	5.1	3.9	6.4	49	4.0	3.0	5.3
	Otitis media acute (10033079)	18	1.5	0.9	2.3	18	1.5	0.9	2.3
	Paronychia (10034016)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Periorbital cellulitis (10057182)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pharyngitis (10034835)	14	1.2	0.6	1.9	15	1.2	0.7	2.0
	Pharyngitis streptococcal (10034839)	2	0.2	0.0	0.6	4	0.3	0.1	0.8
	Pharyngotonsillitis (10049140)	2	0.2	0.0	0.6	5	0.4	0.1	1.0
	Pneumonia (10035664)	2	0.2	0.0	0.6	6	0.5	0.2	1.1
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Pneumonia mycoplasmal (10035724)	3	0.2	0.1	0.7	1	0.1	0.0	0.5
	Pneumonia viral (10035737)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Purulent discharge (10037569)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Rash pustular (10037888)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Respiratory syncytial virus infection (10061603)	2	0.2	0.0	0.6	4	0.3	0.1	0.8
	Respiratory tract infection (10062352)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Respiratory tract infection viral (10062106)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Rhinitis (10039083)	10	0.8	0.4	1.5	6	0.5	0.2	1.1
	Sinusitis (10040753)	6	0.5	0.2	1.1	11	0.9	0.5	1.6

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Skin candida (10054152)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Skin infection (10040872)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Staphylococcal infection (10058080)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Streptococcal infection (10061372)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Tinea capitis (10043866)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Tonsillitis (10044008)	4	0.3	0.1	0.8	6	0.5	0.2	1.1
	Tracheitis (10044302)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Upper respiratory tract infection (10046306)	111	9.2	7.6	11.0	102	8.4	6.9	10.1
	Urinary tract infection (10046571)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Varicella (10046980)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Viral infection (10047461)	9	0.7	0.3	1.4	15	1.2	0.7	2.0
	Viral rash (10047476)	11	0.9	0.5	1.6	5	0.4	0.1	1.0
	Viral upper respiratory tract infection (10047482)	3	0.2	0.1	0.7	7	0.6	0.2	1.2
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Animal bite (10002515)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Arthropod bite (10003399)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Burns second degree (10006802)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Concussion (10010254)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Contusion (10050584)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Corneal abrasion (10010984)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Eyelid contusion (10075018)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Face injury (10050392)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Fall (10016173)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Foreign body (10070245)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Hand fracture (10019114)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Head injury (10019196)	4	0.3	0.1	0.8	2	0.2	0.0	0.6
	Joint dislocation (10023204)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Laceration (10023572)	6	0.5	0.2	1.1	1	0.1	0.0	0.5
	Limb injury (10061225)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Mouth injury (10049294)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Procedural pain (10064882)	0	0.0	0.0	0.3	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Radial head dislocation (10073749)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Rib fracture (10039117)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Scratch (10039737)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Skin abrasion (10064990)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Tooth injury (10044043)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Upper limb fracture (10061394)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Wound (10052428)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
Investigations (10022891)	Blood lead increased (10005642)	4	0.3	0.1	0.8	0	0.0	0.0	0.3
	Body temperature increased (10005911)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Heart rate increased (10019303)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.1	0.0	0.5	5	0.4	0.1	1.0
Musculoskeletal and connective tissue disorders (10028395)	Blount's disease (10072255)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Myalgia (10028411)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Pain in extremity (10033425)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Melanocytic naevus (10027145)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Skin papilloma (10040907)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Nervous system disorders (10029205)	Balance disorder (10049848)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dizziness (10013573)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Febrile convulsion (10016284)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Headache (10019211)	3	0.2	0.1	0.7	3	0.2	0.1	0.7
	Psychomotor hyperactivity (10037211)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Somnolence (10041349)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Speech disorder developmental (10041467)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
Psychiatric disorders (10037175)	Insomnia (10022437)	1	0.1	0.0	0.5	6	0.5	0.2	1.1
	Irritability (10022998)	4	0.3	0.1	0.8	5	0.4	0.1	1.0
	Sleep disorder (10040984)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
Renal and urinary disorders (10038359)	Urinary tract disorder (10046566)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Genital labial adhesions (10064162)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Genital rash (10018175)	1	0.1	0.0	0.5	3	0.2	0.1	0.7

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Asthma (10003553)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Bronchial hyperreactivity (10066091)	3	0.2	0.1	0.7	3	0.2	0.1	0.7
	Bronchospasm (10006482)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Cough (10011224)	70	5.8	4.5	7.3	77	6.3	5.0	7.8
	Dysphonia (10013952)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dyspnoea (10013968)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Epistaxis (10015090)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Nasal congestion (10028735)	25	2.1	1.3	3.0	19	1.6	0.9	2.4
	Nasal discharge discolouration (10071553)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Oropharyngeal pain (10068319)	7	0.6	0.2	1.2	1	0.1	0.0	0.5
	Pulmonary congestion (10037368)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Respiratory disorder (10038683)	6	0.5	0.2	1.1	5	0.4	0.1	1.0
	Respiratory distress (10038687)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Respiratory tract congestion (10052251)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Rhinitis allergic (10039085)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Rhinorrhoea (10039101)	59	4.9	3.7	6.3	76	6.2	5.0	7.8
	Sinus congestion (10040742)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Sinus disorder (10062244)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Sneezing (10041232)	3	0.2	0.1	0.7	10	0.8	0.4	1.5
	Wheezing (10047924)	5	0.4	0.1	1.0	8	0.7	0.3	1.3
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Blister (10005191)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dermal cyst (10012426)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dermatitis (10012431)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Dermatitis acneiform (10012432)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Dermatitis atopic (10012438)	1	0.1	0.0	0.5	5	0.4	0.1	1.0
	Dermatitis contact (10012442)	1	0.1	0.0	0.5	4	0.3	0.1	0.8
	Dermatitis diaper (10012444)	24	2.0	1.3	2.9	13	1.1	0.6	1.8
	Dry skin (10013786)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Ecchymosis (10014080)	1	0.1	0.0	0.5	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
	Eczema (10014184)	0	0.0	0.0	0.3	6	0.5	0.2	1.1
	Erythema (10015150)	2	0.2	0.0	0.6	4	0.3	0.1	0.8
	Hyperhidrosis (10020642)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Keratosis pilaris (10066295)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Night sweats (10029410)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Prurigo (10037083)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pruritus (10037087)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Rash (10037844)	16	1.3	0.8	2.1	13	1.1	0.6	1.8
	Rash erythematous (10037855)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Rash generalised (10037858)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Rash macular (10037867)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Rash papular (10037876)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Rash pruritic (10037884)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Skin fissures (10040849)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Skin irritation (10040880)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Skin lesion (10040882)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Urticaria (10046735)	4	0.3	0.1	0.8	6	0.5	0.2	1.1

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 84 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		637	36.9	34.6	39.2	618	35.4	33.1	37.7
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Iron deficiency anaemia (10022972)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Leukocytosis (10024378)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Lymphadenopathy (10025197)	3	0.2	0.0	0.5	1	0.1	0.0	0.3
	Neutropenia (10029354)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Congenital, familial and genetic disorders (10010331)	Phimosis (10034878)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Tibial torsion (10064515)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	2	0.1	0.0	0.4	5	0.3	0.1	0.7
	Ear discomfort (10052137)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Ear pain (10014020)	6	0.3	0.1	0.8	2	0.1	0.0	0.4
	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Middle ear effusion (10062545)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Dacryostenosis acquired (10053990)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Eye discharge (10015915)	2	0.1	0.0	0.4	2	0.1	0.0	0.4
	Eye pruritus (10052140)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Eyelid oedema (10015993)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Lacrimation increased (10023644)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Photophobia (10034960)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Gastrointestinal disorders (10017947)	Abdominal discomfort (10000059)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Abdominal hernia (10060954)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Abdominal pain upper (10000087)	2	0.1	0.0	0.4	2	0.1	0.0	0.4
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Constipation (10010774)	5	0.3	0.1	0.7	5	0.3	0.1	0.7
	Dental caries (10012318)	3	0.2	0.0	0.5	0	0.0	0.0	0.2
	Diarrhoea (10012735)	72	4.2	3.3	5.2	53	3.0	2.3	4.0
	Faeces hard (10016101)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Flatulence (10016766)	1	0.1	0.0	0.3	3	0.2	0.0	0.5
	Food poisoning (10016952)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Frequent bowel movements (10017367)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Haematochezia (10018836)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Intussusception (10022863)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Nausea (10028813)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Regurgitation (10067171)	0	0.0	0.0	0.2	1	0.1	0.0	0.3

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Stomatitis (10042128)	2	0.1	0.0	0.4	1	0.1	0.0	0.3
	Teething (10043183)	18	1.0	0.6	1.6	22	1.3	0.8	1.9
	Vomiting (10047700)	48	2.8	2.1	3.7	47	2.7	2.0	3.6
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Administration site rash (10071156)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Asthenia (10003549)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Chills (10008531)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Developmental delay (10012559)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Discomfort (10013082)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Fatigue (10016256)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Feeling hot (10016334)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Ill-defined disorder (10061520)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Influenza like illness (10022004)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Injection site bruising (10022052)	2	0.1	0.0	0.4	1	0.1	0.0	0.3
	Injection site pruritus (10022093)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Injection site rash (10022094)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Injection site warmth (10022112)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Local swelling (10024770)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Malaise (10025482)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Pain (10033371)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Pyrexia (10037660)	54	3.1	2.4	4.1	58	3.3	2.5	4.3
	Thirst (10043458)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Vaccination site pain (10068879)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Vaccination site rash (10069482)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Vaccination site reaction (10059080)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Vaccination site swelling (10069620)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Vessel puncture site haemorrhage (10054092)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Immune system disorders (10021428)	Drug hypersensitivity (10013700)	2	0.1	0.0	0.4	2	0.1	0.0	0.4
	Hypersensitivity (10020751)	2	0.1	0.0	0.4	1	0.1	0.0	0.3
	Multiple allergies (10028164)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Seasonal allergy (10048908)	2	0.1	0.0	0.4	1	0.1	0.0	0.3
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Acarodermatitis (10063409)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Acute sinusitis (10001076)	1	0.1	0.0	0.3	5	0.3	0.1	0.7
	Bronchiolitis (10006448)	9	0.5	0.2	1.0	16	0.9	0.5	1.5
	Bronchitis (10006451)	3	0.2	0.0	0.5	9	0.5	0.2	1.0
	Candida infection (10074170)	0	0.0	0.0	0.2	3	0.2	0.0	0.5
	Candida nappy rash (10007135)	4	0.2	0.1	0.6	1	0.1	0.0	0.3
	Cellulitis (10007882)	2	0.1	0.0	0.4	3	0.2	0.0	0.5
	Clostridium difficile infection (10054236)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Conjunctivitis (10010741)	13	0.8	0.4	1.3	20	1.1	0.7	1.8
	Conjunctivitis bacterial (10061784)	1	0.1	0.0	0.3	0	0.0	0.0	0.2

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Coxsackie viral infection (10011261)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Croup infectious (10011416)	15	0.9	0.5	1.4	14	0.8	0.4	1.3
	Dermatophytosis (10012504)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Ear infection (10014011)	10	0.6	0.3	1.1	11	0.6	0.3	1.1
	Enterobiasis (10014881)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Exanthema subitum (10015586)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Eye infection (10015929)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Folliculitis (10016936)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Fungal infection (10017533)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Fungal skin infection (10017543)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Gastroenteritis (10017888)	15	0.9	0.5	1.4	22	1.3	0.8	1.9
	Gastroenteritis viral (10017918)	4	0.2	0.1	0.6	4	0.2	0.1	0.6
	Genital candidiasis (10018143)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Groin abscess (10050269)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Hand-foot-and-mouth disease (10019113)	7	0.4	0.2	0.8	6	0.3	0.1	0.7
	Herpangina (10019936)	1	0.1	0.0	0.3	3	0.2	0.0	0.5
	Impetigo (10021531)	3	0.2	0.0	0.5	1	0.1	0.0	0.3
	Influenza (10022000)	7	0.4	0.2	0.8	7	0.4	0.2	0.8
	Lice infestation (10024424)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Localised infection (10024774)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Lower respiratory tract infection (10024968)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Molluscum contagiosum (10027807)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Nasopharyngitis (10028810)	68	3.9	3.1	5.0	61	3.5	2.7	4.5
	Neonatal candida infection (10028924)	3	0.2	0.0	0.5	0	0.0	0.0	0.2
	Oral candidiasis (10030963)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Otitis externa (10033072)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Otitis media (10033078)	62	3.6	2.8	4.6	51	2.9	2.2	3.8
	Otitis media acute (10033079)	18	1.0	0.6	1.6	18	1.0	0.6	1.6
	Paronychia (10034016)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Periorbital cellulitis (10057182)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Pharyngitis (10034835)	14	0.8	0.4	1.4	15	0.9	0.5	1.4
	Pharyngitis streptococcal (10034839)	2	0.1	0.0	0.4	4	0.2	0.1	0.6
	Pharyngotonsillitis (10049140)	2	0.1	0.0	0.4	5	0.3	0.1	0.7
	Pneumonia (10035664)	2	0.1	0.0	0.4	6	0.3	0.1	0.7
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Pneumonia mycoplasmal (10035724)	3	0.2	0.0	0.5	1	0.1	0.0	0.3
	Pneumonia viral (10035737)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Purulent discharge (10037569)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Rash pustular (10037888)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Respiratory syncytial virus infection (10061603)	2	0.1	0.0	0.4	4	0.2	0.1	0.6
	Respiratory tract infection (10062352)	1	0.1	0.0	0.3	2	0.1	0.0	0.4

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Respiratory tract infection viral (10062106)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Rhinitis (10039083)	10	0.6	0.3	1.1	6	0.3	0.1	0.7
	Sinusitis (10040753)	6	0.3	0.1	0.8	12	0.7	0.4	1.2
	Skin candida (10054152)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Skin infection (10040872)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Staphylococcal infection (10058080)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Streptococcal infection (10061372)	2	0.1	0.0	0.4	2	0.1	0.0	0.4
	Tinea capitis (10043866)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Tonsillitis (10044008)	4	0.2	0.1	0.6	6	0.3	0.1	0.7
	Tracheitis (10044302)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Upper respiratory tract infection (10046306)	114	6.6	5.5	7.9	108	6.2	5.1	7.4
	Urinary tract infection (10046571)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Varicella (10046980)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Viral infection (10047461)	9	0.5	0.2	1.0	15	0.9	0.5	1.4
	Viral rash (10047476)	11	0.6	0.3	1.1	5	0.3	0.1	0.7
	Viral upper respiratory tract infection (10047482)	3	0.2	0.0	0.5	7	0.4	0.2	0.8
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Animal bite (10002515)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Arthropod bite (10003399)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Burns second degree (10006802)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Concussion (10010254)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Contusion (10050584)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Corneal abrasion (10010984)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Eyelid contusion (10075018)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Face injury (10050392)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Fall (10016173)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Foreign body (10070245)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Hand fracture (10019114)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Head injury (10019196)	4	0.2	0.1	0.6	2	0.1	0.0	0.4
	Joint dislocation (10023204)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Laceration (10023572)	6	0.3	0.1	0.8	1	0.1	0.0	0.3
	Limb injury (10061225)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Mouth injury (10049294)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Procedural pain (10064882)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Radial head dislocation (10073749)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Rib fracture (10039117)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Scratch (10039737)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Skin abrasion (10064990)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Tooth injury (10044043)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Upper limb fracture (10061394)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Wound (10052428)	1	0.1	0.0	0.3	1	0.1	0.0	0.3

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Investigations (10022891)	Blood lead increased (10005642)	4	0.2	0.1	0.6	0	0.0	0.0	0.2
	Body temperature increased (10005911)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Heart rate increased (10019303)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.1	0.0	0.3	5	0.3	0.1	0.7
Musculoskeletal and connective tissue disorders (10028395)	Blount's disease (10072255)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Myalgia (10028411)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Pain in extremity (10033425)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Melanocytic naevus (10027145)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Skin papilloma (10040907)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Nervous system disorders (10029205)	Balance disorder (10049848)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Dizziness (10013573)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Febrile convulsion (10016284)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Headache (10019211)	3	0.2	0.0	0.5	3	0.2	0.0	0.5
	Psychomotor hyperactivity (10037211)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Somnolence (10041349)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Speech disorder developmental (10041467)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
Psychiatric disorders (10037175)	Insomnia (10022437)	1	0.1	0.0	0.3	6	0.3	0.1	0.7
	Irritability (10022998)	4	0.2	0.1	0.6	5	0.3	0.1	0.7
	Sleep disorder (10040984)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
Renal and urinary disorders (10038359)	Urinary tract disorder (10046566)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Genital labial adhesions (10064162)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Genital rash (10018175)	1	0.1	0.0	0.3	3	0.2	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Asthma (10003553)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Bronchial hyperreactivity (10066091)	3	0.2	0.0	0.5	3	0.2	0.0	0.5
	Bronchospasm (10006482)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Cough (10011224)	72	4.2	3.3	5.2	78	4.5	3.5	5.5
	Dysphonia (10013952)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Dyspnoea (10013968)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Epistaxis (10015090)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Nasal congestion (10028735)	25	1.4	0.9	2.1	19	1.1	0.7	1.7
	Nasal discharge discolouration (10071553)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Oropharyngeal pain (10068319)	7	0.4	0.2	0.8	1	0.1	0.0	0.3
	Pulmonary congestion (10037368)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Respiratory disorder (10038683)	6	0.3	0.1	0.8	5	0.3	0.1	0.7

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Respiratory distress (10038687)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Respiratory tract congestion (10052251)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Rhinitis allergic (10039085)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Rhinorrhoea (10039101)	60	3.5	2.7	4.5	78	4.5	3.5	5.5
	Sinus congestion (10040742)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Sinus disorder (10062244)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Sneezing (10041232)	3	0.2	0.0	0.5	10	0.6	0.3	1.1
	Wheezing (10047924)	5	0.3	0.1	0.7	8	0.5	0.2	0.9
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Blister (10005191)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Dermal cyst (10012426)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Dermatitis (10012431)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Dermatitis acneiform (10012432)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Dermatitis atopic (10012438)	1	0.1	0.0	0.3	5	0.3	0.1	0.7
	Dermatitis contact (10012442)	1	0.1	0.0	0.3	4	0.2	0.1	0.6
	Dermatitis diaper (10012444)	26	1.5	1.0	2.2	13	0.7	0.4	1.3
	Dry skin (10013786)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Ecchymosis (10014080)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Eczema (10014184)	0	0.0	0.0	0.2	6	0.3	0.1	0.7
	Erythema (10015150)	2	0.1	0.0	0.4	4	0.2	0.1	0.6
	Hyperhidrosis (10020642)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Keratosis pilaris (10066295)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Night sweats (10029410)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Prurigo (10037083)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Pruritus (10037087)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Rash (10037844)	16	0.9	0.5	1.5	14	0.8	0.4	1.3
	Rash erythematous (10037855)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Rash generalised (10037858)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Rash macular (10037867)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Rash papular (10037876)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Rash pruritic (10037884)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Skin fissures (10040849)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Skin irritation (10040880)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Skin lesion (10040882)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Urticaria (10046735)	4	0.2	0.1	0.6	6	0.3	0.1	0.7

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 85 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		70	5.8	4.5	7.3	75	6.2	4.9	7.7
Ear and labyrinth disorders (10013993)	Middle ear effusion (10062545)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Eye discharge (10015915)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Diarrhoea (10012735)	3	0.2	0.1	0.7	6	0.5	0.2	1.1
	Intussusception (10022863)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Nausea (10028813)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Stomatitis (10042128)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Vomiting (10047700)	9	0.7	0.3	1.4	13	1.1	0.6	1.8
General disorders and administration site conditions (10018065)	Chills (10008531)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Injection site pruritus (10022093)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pain (10033371)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pyrexia (10037660)	12	1.0	0.5	1.7	13	1.1	0.6	1.8
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Bronchiolitis (10006448)	2	0.2	0.0	0.6	5	0.4	0.1	1.0
	Candida infection (10074170)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Cellulitis (10007882)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Conjunctivitis (10010741)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Croup infectious (10011416)	5	0.4	0.1	1.0	4	0.3	0.1	0.8
	Ear infection (10014011)	3	0.2	0.1	0.7	2	0.2	0.0	0.6
	Gastroenteritis (10017888)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Gastroenteritis viral (10017918)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Groin abscess (10050269)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Hand-foot-and-mouth disease (10019113)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Herpangina (10019936)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Influenza (10022000)	2	0.2	0.0	0.6	2	0.2	0.0	0.6
	Nasopharyngitis (10028810)	3	0.2	0.1	0.7	5	0.4	0.1	1.0
	Otitis media (10033078)	10	0.8	0.4	1.5	6	0.5	0.2	1.1
	Otitis media acute (10033079)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Pharyngitis (10034835)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Pneumonia (10035664)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Pneumonia mycoplasmal (10035724)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Rhinitis (10039083)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Sinusitis (10040753)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Staphylococcal infection (10058080)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Tonsillitis (10044008)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Upper respiratory tract infection (10046306)	10	0.8	0.4	1.5	7	0.6	0.2	1.2
	Viral infection (10047461)	2	0.2	0.0	0.6	3	0.2	0.1	0.7
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	0.3	2	0.2	0.0	0.6

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Injury, poisoning and procedural complications (10022117)	Face injury (10050392)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Hand fracture (10019114)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Laceration (10023572)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Mouth injury (10049294)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Radial head dislocation (10073749)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Investigations (10022891)	Heart rate increased (10019303)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Headache (10019211)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Somnolence (10041349)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.3	3	0.2	0.1	0.7
	Irritability (10022998)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Cough (10011224)	4	0.3	0.1	0.8	6	0.5	0.2	1.1
	Dyspnoea (10013968)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Nasal congestion (10028735)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Oropharyngeal pain (10068319)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Respiratory disorder (10038683)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Rhinorrhoea (10039101)	1	0.1	0.0	0.5	4	0.3	0.1	0.8
	Wheezing (10047924)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Dermatitis diaper (10012444)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Rash (10037844)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Urticaria (10046735)	1	0.1	0.0	0.5	2	0.2	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 86 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		72	4.2	3.3	5.2	79	4.5	3.6	5.6
Ear and labyrinth disorders (10013993)	Middle ear effusion (10062545)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Eye discharge (10015915)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Diarrhoea (10012735)	3	0.2	0.0	0.5	6	0.3	0.1	0.7
	Intussusception (10022863)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Nausea (10028813)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Stomatitis (10042128)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Vomiting (10047700)	9	0.5	0.2	1.0	13	0.7	0.4	1.3
General disorders and administration site conditions (10018065)	Chills (10008531)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Injection site pruritus (10022093)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Pain (10033371)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Pyrexia (10037660)	12	0.7	0.4	1.2	14	0.8	0.4	1.3
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Bronchiolitis (10006448)	2	0.1	0.0	0.4	5	0.3	0.1	0.7
	Candida infection (10074170)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Cellulitis (10007882)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Conjunctivitis (10010741)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Croup infectious (10011416)	5	0.3	0.1	0.7	4	0.2	0.1	0.6
	Ear infection (10014011)	3	0.2	0.0	0.5	2	0.1	0.0	0.4
	Gastroenteritis (10017888)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Gastroenteritis viral (10017918)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Groin abscess (10050269)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Hand-foot-and-mouth disease (10019113)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Herpangina (10019936)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Influenza (10022000)	2	0.1	0.0	0.4	2	0.1	0.0	0.4
	Nasopharyngitis (10028810)	3	0.2	0.0	0.5	5	0.3	0.1	0.7
	Otitis media (10033078)	10	0.6	0.3	1.1	6	0.3	0.1	0.7
	Otitis media acute (10033079)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Pharyngitis (10034835)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Pneumonia (10035664)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Pneumonia mycoplasmal (10035724)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Rhinitis (10039083)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Sinusitis (10040753)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Staphylococcal infection (10058080)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Tonsillitis (10044008)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Upper respiratory tract infection (10046306)	10	0.6	0.3	1.1	7	0.4	0.2	0.8
	Viral infection (10047461)	2	0.1	0.0	0.4	3	0.2	0.0	0.5
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	0.2	2	0.1	0.0	0.4

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Injury, poisoning and procedural complications (10022117)	Face injury (10050392)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Hand fracture (10019114)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Laceration (10023572)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Mouth injury (10049294)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Radial head dislocation (10073749)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Investigations (10022891)	Heart rate increased (10019303)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
Nervous system disorders (10029205)	Febrile convulsion (10016284)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Headache (10019211)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Somnolence (10041349)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.2	3	0.2	0.0	0.5
	Irritability (10022998)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Cough (10011224)	4	0.2	0.1	0.6	6	0.3	0.1	0.7
	Dyspnoea (10013968)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Nasal congestion (10028735)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Oropharyngeal pain (10068319)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Respiratory disorder (10038683)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Rhinorrhoea (10039101)	1	0.1	0.0	0.3	4	0.2	0.1	0.6
	Wheezing (10047924)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Dermatitis diaper (10012444)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Rash (10037844)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Urticaria (10046735)	1	0.1	0.0	0.3	2	0.1	0.0	0.4

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 87 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		71	5.9	4.6	7.4	71	5.8	4.6	7.3
Blood and lymphatic system disorders (10005329)	Lymphadenopathy (10025197)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Ear and labyrinth disorders (10013993)	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Lacrimation increased (10023644)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Diarrhoea (10012735)	12	1.0	0.5	1.7	13	1.1	0.6	1.8
	Vomiting (10047700)	13	1.1	0.6	1.8	13	1.1	0.6	1.8
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Administration site rash (10071156)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Chills (10008531)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Feeling hot (10016334)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Injection site bruising (10022052)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Injection site rash (10022094)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Injection site warmth (10022112)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Local swelling (10024770)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Malaise (10025482)	2	0.2	0.0	0.6	0	0.0	0.0	0.3
	Pain (10033371)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Pyrexia (10037660)	2	0.2	0.0	0.6	4	0.3	0.1	0.8
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Immune system disorders (10021428)	Multiple allergies (10028164)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Infections and infestations (10021881)	Conjunctivitis (10010741)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Croup infectious (10011416)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Influenza (10022000)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Nasopharyngitis (10028810)	5	0.4	0.1	1.0	3	0.2	0.1	0.7
	Otitis media (10033078)	1	0.1	0.0	0.5	2	0.2	0.0	0.6
	Pharyngitis (10034835)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Rhinitis (10039083)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Upper respiratory tract infection (10046306)	9	0.7	0.3	1.4	4	0.3	0.1	0.8
	Viral infection (10047461)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Nervous system disorders (10029205)	Headache (10019211)	2	0.2	0.0	0.6	1	0.1	0.0	0.5
	Somnolence (10041349)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Irritability (10022998)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	6	0.5	0.2	1.1	12	1.0	0.5	1.7
	Nasal congestion (10028735)	3	0.2	0.1	0.7	7	0.6	0.2	1.2
	Rhinorrhoea (10039101)	9	0.7	0.3	1.4	15	1.2	0.7	2.0
	Sneezing (10041232)	1	0.1	0.0	0.5	3	0.2	0.1	0.7
	Wheezing (10047924)	1	0.1	0.0	0.5	1	0.1	0.0	0.5

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Skin and subcutaneous tissue disorders (10040785)	Dermatitis acneiform (10012432)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Dermatitis diaper (10012444)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Erythema (10015150)	0	0.0	0.0	0.3	2	0.2	0.0	0.6
	Hyperhidrosis (10020642)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Rash (10037844)	6	0.5	0.2	1.1	0	0.0	0.0	0.3
	Rash generalised (10037858)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Rash papular (10037876)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Skin fissures (10040849)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Urticaria (10046735)	1	0.1	0.0	0.5	3	0.2	0.1	0.7

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 88 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		75	4.3	3.4	5.4	73	4.2	3.3	5.2
Blood and lymphatic system disorders (10005329)	Lymphadenopathy (10025197)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Ear and labyrinth disorders (10013993)	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Lacrimation increased (10023644)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Diarrhoea (10012735)	13	0.8	0.4	1.3	13	0.7	0.4	1.3
	Vomiting (10047700)	13	0.8	0.4	1.3	13	0.7	0.4	1.3
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Administration site rash (10071156)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Chills (10008531)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Feeling hot (10016334)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Injection site bruising (10022052)	2	0.1	0.0	0.4	1	0.1	0.0	0.3
	Injection site rash (10022094)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Injection site warmth (10022112)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Local swelling (10024770)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Malaise (10025482)	2	0.1	0.0	0.4	0	0.0	0.0	0.2
	Pain (10033371)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Pyrexia (10037660)	2	0.1	0.0	0.4	4	0.2	0.1	0.6
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Immune system disorders (10021428)	Multiple allergies (10028164)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Infections and infestations (10021881)	Conjunctivitis (10010741)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Croup infectious (10011416)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Influenza (10022000)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Nasopharyngitis (10028810)	5	0.3	0.1	0.7	3	0.2	0.0	0.5
	Otitis media (10033078)	1	0.1	0.0	0.3	2	0.1	0.0	0.4
	Pharyngitis (10034835)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Rhinitis (10039083)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Upper respiratory tract infection (10046306)	9	0.5	0.2	1.0	4	0.2	0.1	0.6
	Viral infection (10047461)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Nervous system disorders (10029205)	Headache (10019211)	2	0.1	0.0	0.4	1	0.1	0.0	0.3
	Somnolence (10041349)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Irritability (10022998)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	6	0.3	0.1	0.8	12	0.7	0.4	1.2
	Nasal congestion (10028735)	3	0.2	0.0	0.5	7	0.4	0.2	0.8
	Rhinorrhoea (10039101)	9	0.5	0.2	1.0	16	0.9	0.5	1.5
	Sneezing (10041232)	1	0.1	0.0	0.3	3	0.2	0.0	0.5
	Wheezing (10047924)	1	0.1	0.0	0.3	1	0.1	0.0	0.3

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Skin and subcutaneous tissue disorders (10040785)	Dermatitis acneiform (10012432)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Dermatitis diaper (10012444)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Erythema (10015150)	0	0.0	0.0	0.2	2	0.1	0.0	0.4
	Hyperhidrosis (10020642)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Rash (10037844)	6	0.3	0.1	0.8	0	0.0	0.0	0.2
	Rash generalised (10037858)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Rash papular (10037876)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Skin fissures (10040849)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Urticaria (10046735)	1	0.1	0.0	0.3	3	0.2	0.0	0.5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 89 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1207				F-QIV N = 1217			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		7	0.6	0.2	1.2	9	0.7	0.3	1.4
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
	Vomiting (10047700)	2	0.2	0.0	0.6	3	0.2	0.1	0.7
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	1	0.1	0.0	0.5	1	0.1	0.0	0.5
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Nasopharyngitis (10028810)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Otitis media (10033078)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Upper respiratory tract infection (10046306)	1	0.1	0.0	0.5	0	0.0	0.0	0.3
	Viral infection (10047461)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Nervous system disorders (10029205)	Somnolence (10041349)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Irritability (10022998)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Rhinorrhoea (10039101)	0	0.0	0.0	0.3	1	0.1	0.0	0.5
	Wheezing (10047924)	1	0.1	0.0	0.5	0	0.0	0.0	0.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 90 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period (Total vaccinated cohort)

		Q-QIV N = 1726				F-QIV N = 1746			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		7	0.4	0.2	0.8	9	0.5	0.2	1.0
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
	Vomiting (10047700)	2	0.1	0.0	0.4	3	0.2	0.0	0.5
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	1	0.1	0.0	0.3	1	0.1	0.0	0.3
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Nasopharyngitis (10028810)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Otitis media (10033078)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Upper respiratory tract infection (10046306)	1	0.1	0.0	0.3	0	0.0	0.0	0.2
	Viral infection (10047461)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Nervous system disorders (10029205)	Somnolence (10041349)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Irritability (10022998)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Rhinorrhoea (10039101)	0	0.0	0.0	0.2	1	0.1	0.0	0.3
	Wheezing (10047924)	1	0.1	0.0	0.3	0	0.0	0.0	0.2

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 91 Incidence of concomitant medication use during the entire study period by dose and overall (Total vaccinated cohort)

	Q-QIV					F-QIV				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
Any	1207	625	51.8	48.9	54.6	1217	624	51.3	48.4	54.1
Any antipyretic	1207	408	33.8	31.1	36.5	1217	384	31.6	28.9	34.2
Prophylactic antipyretic	1207	30	2.5	1.7	3.5	1217	23	1.9	1.2	2.8
Any antibiotic	1207	248	20.5	18.3	22.9	1217	238	19.6	17.4	21.9
Prophylactic antibiotic	1207	0	0.0	0.0	0.3	1217	0	0.0	0.0	0.3
Dose 2										
Any	519	256	49.3	44.9	53.7	529	274	51.8	47.4	56.1
Any antipyretic	519	151	29.1	25.2	33.2	529	179	33.8	29.8	38.0
Prophylactic antipyretic	519	5	1.0	0.3	2.2	529	5	0.9	0.3	2.2
Any antibiotic	519	122	23.5	19.9	27.4	529	141	26.7	22.9	30.6
Prophylactic antibiotic	519	0	0.0	0.0	0.7	529	0	0.0	0.0	0.7
Overall/dose										
Any	1726	881	51.0	48.7	53.4	1746	898	51.4	49.1	53.8
Any antipyretic	1726	559	32.4	30.2	34.7	1746	563	32.2	30.1	34.5
Prophylactic antipyretic	1726	35	2.0	1.4	2.8	1746	28	1.6	1.1	2.3
Any antibiotic	1726	370	21.4	19.5	23.4	1746	379	21.7	19.8	23.7
Prophylactic antibiotic	1726	0	0.0	0.0	0.2	1746	0	0.0	0.0	0.2
Overall/subject										
Any	1207	728	60.3	57.5	63.1	1217	737	60.6	57.7	63.3
Any antipyretic	1207	477	39.5	36.7	42.3	1217	474	38.9	36.2	41.8
Prophylactic antipyretic	1207	32	2.7	1.8	3.7	1217	26	2.1	1.4	3.1
Any antibiotic	1207	341	28.3	25.7	30.9	1217	352	28.9	26.4	31.6
Prophylactic antibiotic	1207	0	0.0	0.0	0.3	1217	0	0.0	0.0	0.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N = number of administered doses
n/% = number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 92 Overall number and percentage of subjects who received concomitant vaccination on the same day as the study vaccine (Total vaccinated cohort)

	Q-QIV					F-QIV				
				95% CI					95% CI	
Concomitant vaccination	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
At least one concomitant vaccination	1207	260	21.5	19.3	24.0	1217	246	20.2	18.0	22.6
DTaP	1207	57	4.7	3.6	6.1	1217	52	4.3	3.2	5.6
DTaP-Hep B-IPV	1207	31	2.6	1.8	3.6	1217	28	2.3	1.5	3.3
DTaP-Hib-IPV	1207	52	4.3	3.2	5.6	1217	59	4.8	3.7	6.2
Hep A	1207	114	9.4	7.9	11.2	1217	103	8.5	7.0	10.2
Hep B	1207	30	2.5	1.7	3.5	1217	33	2.7	1.9	3.8
Hib	1207	81	6.7	5.4	8.3	1217	77	6.3	5.0	7.8
IPV	1207	17	1.4	0.8	2.2	1217	18	1.5	0.9	2.3
Influenza	1207	1	0.1	0.0	0.5	1217	0	0.0	0.0	0.3
MMR	1207	43	3.6	2.6	4.8	1217	35	2.9	2.0	4.0
MMRV	1207	9	0.7	0.3	1.4	1217	10	0.8	0.4	1.5
OPV	1207	0	0.0	0.0	0.3	1217	0	0.0	0.0	0.3
PCV	1207	19	1.6	1.0	2.4	1217	14	1.2	0.6	1.9
PCV 13	1207	107	8.9	7.3	10.6	1217	105	8.6	7.1	10.3
Polio	1207	1	0.1	0.0	0.5	1217	1	0.1	0.0	0.5
Rotavirus	1207	45	3.7	2.7	5.0	1217	57	4.7	3.6	6.0
Varicella	1207	50	4.1	3.1	5.4	1217	34	2.8	1.9	3.9
pneummococcal	1207	9	0.7	0.3	1.4	1217	2	0.2	0.0	0.6
Dose 2										
At least one concomitant vaccination	519	36	6.9	4.9	9.5	529	16	3.0	1.7	4.9
DTaP	519	7	1.3	0.5	2.8	529	3	0.6	0.1	1.6
DTaP-Hep B-IPV	519	1	0.2	0.0	1.1	529	1	0.2	0.0	1.0
DTaP-Hib-IPV	519	4	0.8	0.2	2.0	529	1	0.2	0.0	1.0
Hep A	519	10	1.9	0.9	3.5	529	3	0.6	0.1	1.6
Hep B	519	7	1.3	0.5	2.8	529	2	0.4	0.0	1.4
Hib	519	8	1.5	0.7	3.0	529	3	0.6	0.1	1.6
IPV	519	1	0.2	0.0	1.1	529	0	0.0	0.0	0.7
Influenza	519	0	0.0	0.0	0.7	529	0	0.0	0.0	0.7
MMR	519	10	1.9	0.9	3.5	529	2	0.4	0.0	1.4
MMRV	519	0	0.0	0.0	0.7	529	1	0.2	0.0	1.0
OPV	519	0	0.0	0.0	0.7	529	0	0.0	0.0	0.7
PCV	519	0	0.0	0.0	0.7	529	0	0.0	0.0	0.7
PCV 13	519	15	2.9	1.6	4.7	529	10	1.9	0.9	3.4
Polio	519	1	0.2	0.0	1.1	529	0	0.0	0.0	0.7
Rotavirus	519	2	0.4	0.0	1.4	529	1	0.2	0.0	1.0
Varicella	519	9	1.7	0.8	3.3	529	1	0.2	0.0	1.0
pneummococcal	519	3	0.6	0.1	1.7	529	0	0.0	0.0	0.7
Overall/dose										
At least one concomitant vaccination	1726	744	43.1	40.8	45.5	1746	656	37.6	35.3	39.9
DTaP	1726	64	3.7	2.9	4.7	1746	55	3.2	2.4	4.1
DTaP-Hep B-IPV	1726	32	1.9	1.3	2.6	1746	29	1.7	1.1	2.4
DTaP-Hib-IPV	1726	56	3.2	2.5	4.2	1746	60	3.4	2.6	4.4
Hep A	1726	124	7.2	6.0	8.5	1746	106	6.1	5.0	7.3
Hep B	1726	37	2.1	1.5	2.9	1746	35	2.0	1.4	2.8
Hib	1726	89	5.2	4.2	6.3	1746	80	4.6	3.6	5.7
IPV	1726	18	1.0	0.6	1.6	1746	18	1.0	0.6	1.6
Influenza	1726	1	0.1	0.0	0.3	1746	0	0.0	0.0	0.2
MMR	1726	53	3.1	2.3	4.0	1746	37	2.1	1.5	2.9

	Q-QIV					F-QIV				
				95% CI					95% CI	
Concomitant vaccination	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
MMRV	1726	9	0.5	0.2	1.0	1746	11	0.6	0.3	1.1
OPV	1726	0	0.0	0.0	0.2	1746	0	0.0	0.0	0.2
PCV	1726	19	1.1	0.7	1.7	1746	14	0.8	0.4	1.3
PCV 13	1726	122	7.1	5.9	8.4	1746	115	6.6	5.5	7.9
Polio	1726	2	0.1	0.0	0.4	1746	1	0.1	0.0	0.3
Rotavirus	1726	47	2.7	2.0	3.6	1746	58	3.3	2.5	4.3
Varicella	1726	59	3.4	2.6	4.4	1746	35	2.0	1.4	2.8
pneummococcal	1726	12	0.7	0.4	1.2	1746	2	0.1	0.0	0.4
Overall/subject										
At least one concomitant vaccination	1207	282	23.4	21.0	25.9	1217	250	20.5	18.3	22.9
DTaP	1207	64	5.3	4.1	6.7	1217	55	4.5	3.4	5.8
DTaP-Hep B-IPV	1207	32	2.7	1.8	3.7	1217	29	2.4	1.6	3.4
DTaP-Hib-IPV	1207	56	4.6	3.5	6.0	1217	60	4.9	3.8	6.3
Hep A	1207	124	10.3	8.6	12.1	1217	106	8.7	7.2	10.4
Hep B	1207	37	3.1	2.2	4.2	1217	35	2.9	2.0	4.0
Hib	1207	89	7.4	6.0	9.0	1217	80	6.6	5.2	8.1
IPV	1207	18	1.5	0.9	2.3	1217	18	1.5	0.9	2.3
Influenza	1207	1	0.1	0.0	0.5	1217	0	0.0	0.0	0.3
MMR	1207	53	4.4	3.3	5.7	1217	37	3.0	2.1	4.2
MMRV	1207	9	0.7	0.3	1.4	1217	11	0.9	0.5	1.6
OPV	1207	0	0.0	0.0	0.3	1217	0	0.0	0.0	0.3
PCV	1207	19	1.6	1.0	2.4	1217	14	1.2	0.6	1.9
PCV 13	1207	122	10.1	8.5	11.9	1217	115	9.4	7.9	11.2
Polio	1207	2	0.2	0.0	0.6	1217	1	0.1	0.0	0.5
Rotavirus	1207	47	3.9	2.9	5.1	1217	58	4.8	3.6	6.1
Varicella	1207	59	4.9	3.7	6.3	1217	35	2.9	2.0	4.0
pneummococcal	1207	12	1.0	0.5	1.7	1217	2	0.2	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects with a concomitant vaccination
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses with a concomitant vaccination
95%CI = Exact 95% confidence interval: LL = lower limit, UL = upper limit

Table 93 Overall number and percentage of subjects who received concomitant vaccination within 7 days of the study vaccine (Total vaccinated cohort)

	Q-QIV					F-QIV				
				95% CI					95% CI	
Concomitant vaccination	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
At least one concomitant vaccination	1207	268	22.2	19.9	24.7	1217	258	21.2	18.9	23.6
DTaP	1207	59	4.9	3.7	6.3	1217	55	4.5	3.4	5.8
DTaP-Hep B-IPV	1207	31	2.6	1.8	3.6	1217	29	2.4	1.6	3.4
DTaP-Hib-IPV	1207	53	4.4	3.3	5.7	1217	61	5.0	3.9	6.4
Hep A	1207	118	9.8	8.2	11.6	1217	110	9.0	7.5	10.8
Hep B	1207	33	2.7	1.9	3.8	1217	34	2.8	1.9	3.9
Hib	1207	83	6.9	5.5	8.5	1217	79	6.5	5.2	8.0
IPV	1207	17	1.4	0.8	2.2	1217	20	1.6	1.0	2.5
Influenza	1207	1	0.1	0.0	0.5	1217	0	0.0	0.0	0.3
MMR	1207	45	3.7	2.7	5.0	1217	36	3.0	2.1	4.1
MMRV	1207	10	0.8	0.4	1.5	1217	11	0.9	0.5	1.6
OPV	1207	0	0.0	0.0	0.3	1217	0	0.0	0.0	0.3
PCV	1207	19	1.6	1.0	2.4	1217	14	1.2	0.6	1.9
PCV 13	1207	109	9.0	7.5	10.8	1217	107	8.8	7.3	10.5
Polio	1207	2	0.2	0.0	0.6	1217	1	0.1	0.0	0.5
Rotavirus	1207	46	3.8	2.8	5.1	1217	57	4.7	3.6	6.0
Varicella	1207	52	4.3	3.2	5.6	1217	35	2.9	2.0	4.0
pneummococcal	1207	11	0.9	0.5	1.6	1217	2	0.2	0.0	0.6
Dose 2										
At least one concomitant vaccination	519	39	7.5	5.4	10.1	529	19	3.6	2.2	5.6
DTaP	519	7	1.3	0.5	2.8	529	3	0.6	0.1	1.6
DTaP-Hep B-IPV	519	1	0.2	0.0	1.1	529	1	0.2	0.0	1.0
DTaP-Hib-IPV	519	4	0.8	0.2	2.0	529	1	0.2	0.0	1.0
Hep A	519	12	2.3	1.2	4.0	529	4	0.8	0.2	1.9
Hep B	519	7	1.3	0.5	2.8	529	3	0.6	0.1	1.6
Hib	519	9	1.7	0.8	3.3	529	4	0.8	0.2	1.9
IPV	519	2	0.4	0.0	1.4	529	0	0.0	0.0	0.7
Influenza	519	0	0.0	0.0	0.7	529	0	0.0	0.0	0.7
MMR	519	11	2.1	1.1	3.8	529	4	0.8	0.2	1.9
MMRV	519	0	0.0	0.0	0.7	529	1	0.2	0.0	1.0
OPV	519	0	0.0	0.0	0.7	529	0	0.0	0.0	0.7
PCV	519	1	0.2	0.0	1.1	529	0	0.0	0.0	0.7
PCV 13	519	15	2.9	1.6	4.7	529	11	2.1	1.0	3.7
Polio	519	1	0.2	0.0	1.1	529	0	0.0	0.0	0.7
Rotavirus	519	2	0.4	0.0	1.4	529	1	0.2	0.0	1.0
Varicella	519	10	1.9	0.9	3.5	529	3	0.6	0.1	1.6
pneummococcal	519	3	0.6	0.1	1.7	529	0	0.0	0.0	0.7
Overall/dose										
At least one concomitant vaccination	1726	774	44.8	42.5	47.2	1746	687	39.3	37.0	41.7
DTaP	1726	66	3.8	3.0	4.8	1746	58	3.3	2.5	4.3
DTaP-Hep B-IPV	1726	32	1.9	1.3	2.6	1746	30	1.7	1.2	2.4
DTaP-Hib-IPV	1726	57	3.3	2.5	4.3	1746	62	3.6	2.7	4.5
Hep A	1726	130	7.5	6.3	8.9	1746	114	6.5	5.4	7.8
Hep B	1726	40	2.3	1.7	3.1	1746	37	2.1	1.5	2.9
Hib	1726	92	5.3	4.3	6.5	1746	83	4.8	3.8	5.9
IPV	1726	19	1.1	0.7	1.7	1746	20	1.1	0.7	1.8
Influenza	1726	1	0.1	0.0	0.3	1746	0	0.0	0.0	0.2
MMR	1726	56	3.2	2.5	4.2	1746	40	2.3	1.6	3.1

	Q-QIV					F-QIV				
				95% CI					95% CI	
Concomitant vaccination	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
MMRV	1726	10	0.6	0.3	1.1	1746	12	0.7	0.4	1.2
OPV	1726	0	0.0	0.0	0.2	1746	0	0.0	0.0	0.2
PCV	1726	20	1.2	0.7	1.8	1746	14	0.8	0.4	1.3
PCV 13	1726	124	7.2	6.0	8.5	1746	118	6.8	5.6	8.0
Polio	1726	3	0.2	0.0	0.5	1746	1	0.1	0.0	0.3
Rotavirus	1726	48	2.8	2.1	3.7	1746	58	3.3	2.5	4.3
Varicella	1726	62	3.6	2.8	4.6	1746	38	2.2	1.5	3.0
pneummococcal	1726	14	0.8	0.4	1.4	1746	2	0.1	0.0	0.4
Overall/subject										
At least one concomitant vaccination	1207	293	24.3	21.9	26.8	1217	265	21.8	19.5	24.2
DTaP	1207	66	5.5	4.3	6.9	1217	58	4.8	3.6	6.1
DTaP-Hep B-IPV	1207	32	2.7	1.8	3.7	1217	30	2.5	1.7	3.5
DTaP-Hib-IPV	1207	57	4.7	3.6	6.1	1217	62	5.1	3.9	6.5
Hep A	1207	130	10.8	9.1	12.7	1217	114	9.4	7.8	11.1
Hep B	1207	40	3.3	2.4	4.5	1217	37	3.0	2.1	4.2
Hib	1207	92	7.6	6.2	9.3	1217	83	6.8	5.5	8.4
IPV	1207	19	1.6	1.0	2.4	1217	20	1.6	1.0	2.5
Influenza	1207	1	0.1	0.0	0.5	1217	0	0.0	0.0	0.3
MMR	1207	56	4.6	3.5	6.0	1217	40	3.3	2.4	4.4
MMRV	1207	10	0.8	0.4	1.5	1217	12	1.0	0.5	1.7
OPV	1207	0	0.0	0.0	0.3	1217	0	0.0	0.0	0.3
PCV	1207	20	1.7	1.0	2.5	1217	14	1.2	0.6	1.9
PCV 13	1207	124	10.3	8.6	12.1	1217	118	9.7	8.1	11.5
Polio	1207	3	0.2	0.1	0.7	1217	1	0.1	0.0	0.5
Rotavirus	1207	48	4.0	2.9	5.2	1217	58	4.8	3.6	6.1
Varicella	1207	62	5.1	4.0	6.5	1217	38	3.1	2.2	4.3
pneummococcal	1207	14	1.2	0.6	1.9	1217	2	0.2	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects with a concomitant vaccination
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses with a concomitant vaccination
95%CI = Exact 95% confidence interval: LL = lower limit, UL = upper limit

Table 94 Overall number and percentage of subjects who received concomitant vaccination during the entire follow-up period (Total vaccinated cohort)

	Q-QIV					F-QIV				
				95% CI					95% CI	
Concomitant vaccination	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1										
At least one concomitant vaccination	1207	362	30.0	27.4	32.7	1217	361	29.7	27.1	32.3
DTaP	1207	83	6.9	5.5	8.5	1217	80	6.6	5.2	8.1
DTaP-Hep B-IPV	1207	33	2.7	1.9	3.8	1217	31	2.5	1.7	3.6
DTaP-Hib-IPV	1207	60	5.0	3.8	6.4	1217	67	5.5	4.3	6.9
Hep A	1207	197	16.3	14.3	18.5	1217	190	15.6	13.6	17.8
Hep B	1207	36	3.0	2.1	4.1	1217	48	3.9	2.9	5.2
Hib	1207	107	8.9	7.3	10.6	1217	93	7.6	6.2	9.3
IPV	1207	20	1.7	1.0	2.5	1217	26	2.1	1.4	3.1
Influenza	1207	5	0.4	0.1	1.0	1217	6	0.5	0.2	1.1
MMR	1207	60	5.0	3.8	6.4	1217	55	4.5	3.4	5.8
MMRV	1207	11	0.9	0.5	1.6	1217	12	1.0	0.5	1.7
OPV	1207	6	0.5	0.2	1.1	1217	4	0.3	0.1	0.8
PCV	1207	24	2.0	1.3	2.9	1217	19	1.6	0.9	2.4
PCV 13	1207	121	10.0	8.4	11.9	1217	117	9.6	8.0	11.4
Polio	1207	4	0.3	0.1	0.8	1217	2	0.2	0.0	0.6
Rotavirus	1207	47	3.9	2.9	5.1	1217	59	4.8	3.7	6.2
Varicella	1207	66	5.5	4.3	6.9	1217	47	3.9	2.9	5.1
pneummococcal	1207	13	1.1	0.6	1.8	1217	3	0.2	0.1	0.7
Dose 2										
At least one concomitant vaccination	519	240	46.2	41.9	50.6	529	216	40.8	36.6	45.2
DTaP	519	52	10.0	7.6	12.9	529	55	10.4	7.9	13.3
DTaP-Hep B-IPV	519	3	0.6	0.1	1.7	529	2	0.4	0.0	1.4
DTaP-Hib-IPV	519	44	8.5	6.2	11.2	529	34	6.4	4.5	8.9
Hep A	519	116	22.4	18.8	26.2	529	92	17.4	14.3	20.9
Hep B	519	35	6.7	4.7	9.3	529	35	6.6	4.7	9.1
Hib	519	60	11.6	8.9	14.6	529	70	13.2	10.5	16.4
IPV	519	13	2.5	1.3	4.2	529	5	0.9	0.3	2.2
Influenza	519	2	0.4	0.0	1.4	529	1	0.2	0.0	1.0
MMR	519	119	22.9	19.4	26.8	529	96	18.1	15.0	21.7
MMRV	519	13	2.5	1.3	4.2	529	11	2.1	1.0	3.7
OPV	519	8	1.5	0.7	3.0	529	7	1.3	0.5	2.7
PCV	519	9	1.7	0.8	3.3	529	15	2.8	1.6	4.6
PCV 13	519	88	17.0	13.8	20.5	529	84	15.9	12.9	19.3
Polio	519	8	1.5	0.7	3.0	529	4	0.8	0.2	1.9
Rotavirus	519	3	0.6	0.1	1.7	529	3	0.6	0.1	1.6
Varicella	519	102	19.7	16.3	23.3	529	89	16.8	13.7	20.3
pneummococcal	519	21	4.0	2.5	6.1	529	9	1.7	0.8	3.2
Overall/dose										
At least one concomitant vaccination	1726	1600	92.7	91.4	93.9	1746	1479	84.7	82.9	86.4
DTaP	1726	136	7.9	6.7	9.3	1746	136	7.8	6.6	9.1
DTaP-Hep B-IPV	1726	36	2.1	1.5	2.9	1746	33	1.9	1.3	2.6
DTaP-Hib-IPV	1726	104	6.0	4.9	7.3	1746	101	5.8	4.7	7.0
Hep A	1726	313	18.1	16.3	20.0	1746	282	16.2	14.5	18.0
Hep B	1726	72	4.2	3.3	5.2	1746	83	4.8	3.8	5.9
Hib	1726	169	9.8	8.4	11.3	1746	165	9.5	8.1	10.9
IPV	1726	33	1.9	1.3	2.7	1746	31	1.8	1.2	2.5
Influenza	1726	9	0.5	0.2	1.0	1746	7	0.4	0.2	0.8
MMR	1726	179	10.4	9.0	11.9	1746	151	8.6	7.4	10.1

	Q-QIV					F-QIV				
				95% CI					95% CI	
Concomitant vaccination	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
MMRV	1726	24	1.4	0.9	2.1	1746	23	1.3	0.8	2.0
OPV	1726	15	0.9	0.5	1.4	1746	12	0.7	0.4	1.2
PCV	1726	33	1.9	1.3	2.7	1746	34	1.9	1.4	2.7
PCV 13	1726	212	12.3	10.8	13.9	1746	204	11.7	10.2	13.3
Polio	1726	12	0.7	0.4	1.2	1746	6	0.3	0.1	0.7
Rotavirus	1726	50	2.9	2.2	3.8	1746	63	3.6	2.8	4.6
Varicella	1726	169	9.8	8.4	11.3	1746	136	7.8	6.6	9.1
pneummococcal	1726	34	2.0	1.4	2.7	1746	12	0.7	0.4	1.2
Overall/subject										
At least one concomitant vaccination	1207	523	43.3	40.5	46.2	1217	511	42.0	39.2	44.8
DTaP	1207	133	11.0	9.3	12.9	1217	135	11.1	9.4	13.0
DTaP-Hep B-IPV	1207	36	3.0	2.1	4.1	1217	33	2.7	1.9	3.8
DTaP-Hib-IPV	1207	103	8.5	7.0	10.3	1217	101	8.3	6.8	10.0
Hep A	1207	312	25.8	23.4	28.4	1217	282	23.2	20.8	25.6
Hep B	1207	69	5.7	4.5	7.2	1217	83	6.8	5.5	8.4
Hib	1207	164	13.6	11.7	15.7	1217	158	13.0	11.1	15.0
IPV	1207	33	2.7	1.9	3.8	1217	31	2.5	1.7	3.6
Influenza	1207	7	0.6	0.2	1.2	1217	7	0.6	0.2	1.2
MMR	1207	179	14.8	12.9	17.0	1217	149	12.2	10.5	14.2
MMRV	1207	24	2.0	1.3	2.9	1217	23	1.9	1.2	2.8
OPV	1207	14	1.2	0.6	1.9	1217	11	0.9	0.5	1.6
PCV	1207	33	2.7	1.9	3.8	1217	33	2.7	1.9	3.8
PCV 13	1207	200	16.6	14.5	18.8	1217	193	15.9	13.8	18.0
Polio	1207	12	1.0	0.5	1.7	1217	6	0.5	0.2	1.1
Rotavirus	1207	50	4.1	3.1	5.4	1217	62	5.1	3.9	6.5
Varicella	1207	168	13.9	12.0	16.0	1217	134	11.0	9.3	12.9
pneummococcal	1207	34	2.8	2.0	3.9	1217	12	1.0	0.5	1.7

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects with a concomitant vaccination
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses with a concomitant vaccination
95%CI = Exact 95% confidence interval: LL = lower limit, UL = upper limit

Table 95 Incidence of risk factors for complications from Influenza infections (Total vaccinated cohort)

	Q-QIV N = 1207				F-QIV N = 1217			
			95% CI				95% CI	
Symptom	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one risk factor	82	6.8	5.4	8.4	75	6.2	4.9	7.7
Chronic pulmonary disorder including Asthma	54	4.5	3.4	5.8	63	5.2	4.0	6.6
Chronic hepatic disorder	0	0.0	0.0	0.3	0	0.0	0.0	0.3
Chronic renal disorder	2	0.2	0.0	0.6	1	0.1	0.0	0.5
Chronic cardiovascular disorder	10	0.8	0.4	1.5	8	0.7	0.3	1.3
Chronic neurological/neuromuscular conditions	5	0.4	0.1	1.0	2	0.2	0.0	0.6
Chronic hematologic disorder	9	0.7	0.3	1.4	3	0.2	0.1	0.7
Chronic metabolic disorder	4	0.3	0.1	0.8	1	0.1	0.0	0.5
Children receiving long-term aspirin therapy	0	0.0	0.0	0.3	0	0.0	0.0	0.3
Morbidly obese	0	0.0	0.0	0.3	0	0.0	0.0	0.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
N= number of vaccinated subjects
n/%= number/percentage of subjects reporting at least one risk factor
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 96 Incidence and nature of solicited AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	478	352	73.6	69.4	77.5	478	320	66.9	62.5	71.2	478	175	36.6	32.3	41.1
		18-35M	677	455	67.2	63.5	70.7	677	387	57.2	53.3	60.9	673	292	43.4	39.6	47.2
	F-QIV	6-17M	467	334	71.5	67.2	75.6	467	307	65.7	61.2	70.0	465	173	37.2	32.8	41.8
		18-35M	681	450	66.1	62.4	69.6	681	391	57.4	53.6	61.2	681	262	38.5	34.8	42.2
Dose 2	Q-QIV	6-17M	373	230	61.7	56.5	66.6	373	210	56.3	51.1	61.4	373	104	27.9	23.4	32.7
		18-35M	117	64	54.7	45.2	63.9	117	55	47.0	37.7	56.5	117	35	29.9	21.8	39.1
	F-QIV	6-17M	374	236	63.1	58.0	68.0	374	223	59.6	54.5	64.6	372	108	29.0	24.5	33.9
		18-35M	121	62	51.2	42.0	60.4	121	53	43.8	34.8	53.1	121	39	32.2	24.0	41.3
Overall/dose	Q-QIV	6-17M	851	582	68.4	65.1	71.5	851	530	62.3	58.9	65.5	851	279	32.8	29.6	36.1
		18-35M	794	519	65.4	61.9	68.7	794	442	55.7	52.1	59.2	790	327	41.4	37.9	44.9
	F-QIV	6-17M	841	570	67.8	64.5	70.9	841	530	63.0	59.7	66.3	837	281	33.6	30.4	36.9
		18-35M	802	512	63.8	60.4	67.2	802	444	55.4	51.8	58.8	802	301	37.5	34.2	41.0
Overall/subject	Q-QIV	6-17M	481	392	81.5	77.7	84.9	481	366	76.1	72.0	79.8	481	212	44.1	39.6	48.6
		18-35M	678	467	68.9	65.2	72.3	678	402	59.3	55.5	63.0	675	301	44.6	40.8	48.4
	F-QIV	6-17M	470	362	77.0	72.9	80.8	470	345	73.4	69.2	77.3	469	196	41.8	37.3	46.4
		18-35M	682	463	67.9	64.2	71.4	682	404	59.2	55.4	63.0	682	272	39.9	36.2	43.7

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 97 Incidence and nature of solicited grade 3 AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	478	48	10.0	7.5	13.1	478	42	8.8	6.4	11.7	478	11	2.3	1.2	4.1
		18-35M	677	51	7.5	5.7	9.8	677	40	5.9	4.3	8.0	673	17	2.5	1.5	4.0
	F-QIV	6-17M	467	37	7.9	5.6	10.8	467	33	7.1	4.9	9.8	465	12	2.6	1.3	4.5
		18-35M	681	41	6.0	4.4	8.1	681	38	5.6	4.0	7.6	681	4	0.6	0.2	1.5
Dose 2	Q-QIV	6-17M	373	28	7.5	5.0	10.7	373	25	6.7	4.4	9.7	373	6	1.6	0.6	3.5
		18-35M	117	12	10.3	5.4	17.2	117	9	7.7	3.6	14.1	117	3	2.6	0.5	7.3
	F-QIV	6-17M	374	15	4.0	2.3	6.5	374	15	4.0	2.3	6.5	372	1	0.3	0.0	1.5
		18-35M	121	9	7.4	3.5	13.7	121	7	5.8	2.4	11.6	121	2	1.7	0.2	5.8
Overall/dose	Q-QIV	6-17M	851	76	8.9	7.1	11.1	851	67	7.9	6.2	9.9	851	17	2.0	1.2	3.2
		18-35M	794	63	7.9	6.2	10.0	794	49	6.2	4.6	8.1	790	20	2.5	1.6	3.9
	F-QIV	6-17M	841	52	6.2	4.7	8.0	841	48	5.7	4.2	7.5	837	13	1.6	0.8	2.6
		18-35M	802	50	6.2	4.7	8.1	802	45	5.6	4.1	7.4	802	6	0.7	0.3	1.6
Overall/subject	Q-QIV	6-17M	481	67	13.9	11.0	17.3	481	60	12.5	9.7	15.8	481	15	3.1	1.8	5.1
		18-35M	678	61	9.0	7.0	11.4	678	49	7.2	5.4	9.4	675	19	2.8	1.7	4.4
	F-QIV	6-17M	470	46	9.8	7.3	12.8	470	42	8.9	6.5	11.9	469	13	2.8	1.5	4.7
		18-35M	682	47	6.9	5.1	9.1	682	42	6.2	4.5	8.2	682	6	0.9	0.3	1.9

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 98 Incidence and nature of solicited AEs with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	478	322	67.4	63.0	71.6	478	272	56.9	52.3	61.4	478	175	36.6	32.3	41.1
		18-35M	677	418	61.7	58.0	65.4	677	324	47.9	44.0	51.7	673	292	43.4	39.6	47.2
	F-QIV	6-17M	467	306	65.5	61.0	69.8	467	262	56.1	51.5	60.7	465	173	37.2	32.8	41.8
		18-35M	681	410	60.2	56.4	63.9	681	333	48.9	45.1	52.7	681	262	38.5	34.8	42.2
Dose 2	Q-QIV	6-17M	373	210	56.3	51.1	61.4	373	182	48.8	43.6	54.0	373	104	27.9	23.4	32.7
		18-35M	117	55	47.0	37.7	56.5	117	40	34.2	25.7	43.5	117	35	29.9	21.8	39.1
	F-QIV	6-17M	374	204	54.5	49.3	59.7	374	176	47.1	41.9	52.3	372	108	29.0	24.5	33.9
		18-35M	121	56	46.3	37.2	55.6	121	44	36.4	27.8	45.6	121	39	32.2	24.0	41.3
Overall/dose	Q-QIV	6-17M	851	532	62.5	59.2	65.8	851	454	53.3	49.9	56.7	851	279	32.8	29.6	36.1
		18-35M	794	473	59.6	56.1	63.0	794	364	45.8	42.3	49.4	790	327	41.4	37.9	44.9
	F-QIV	6-17M	841	510	60.6	57.2	64.0	841	438	52.1	48.6	55.5	837	281	33.6	30.4	36.9
		18-35M	802	466	58.1	54.6	61.5	802	377	47.0	43.5	50.5	802	301	37.5	34.2	41.0
Overall/subject	Q-QIV	6-17M	481	361	75.1	70.9	78.9	481	316	65.7	61.3	69.9	481	212	44.1	39.6	48.6
		18-35M	678	429	63.3	59.5	66.9	678	338	49.9	46.0	53.7	675	301	44.6	40.8	48.4
	F-QIV	6-17M	470	335	71.3	67.0	75.3	470	300	63.8	59.3	68.2	469	196	41.8	37.3	46.4
		18-35M	682	422	61.9	58.1	65.5	682	344	50.4	46.6	54.3	682	272	39.9	36.2	43.7

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 99 Incidence and nature of solicited grade 3 AEs with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	6-17M	478	40	8.4	6.0	11.2	478	33	6.9	4.8	9.6	478	11	2.3	1.2	4.1
		18-35M	677	46	6.8	5.0	9.0	677	32	4.7	3.3	6.6	673	17	2.5	1.5	4.0
	F-QIV	6-17M	467	36	7.7	5.5	10.5	467	32	6.9	4.7	9.5	465	12	2.6	1.3	4.5
		18-35M	681	34	5.0	3.5	6.9	681	31	4.6	3.1	6.4	681	4	0.6	0.2	1.5
Dose 2	Q-QIV	6-17M	373	20	5.4	3.3	8.2	373	17	4.6	2.7	7.2	373	6	1.6	0.6	3.5
		18-35M	117	12	10.3	5.4	17.2	117	9	7.7	3.6	14.1	117	3	2.6	0.5	7.3
	F-QIV	6-17M	374	8	2.1	0.9	4.2	374	8	2.1	0.9	4.2	372	1	0.3	0.0	1.5
		18-35M	121	6	5.0	1.8	10.5	121	4	3.3	0.9	8.2	121	2	1.7	0.2	5.8
Overall/dose	Q-QIV	6-17M	851	60	7.1	5.4	9.0	851	50	5.9	4.4	7.7	851	17	2.0	1.2	3.2
		18-35M	794	58	7.3	5.6	9.3	794	41	5.2	3.7	6.9	790	20	2.5	1.6	3.9
	F-QIV	6-17M	841	44	5.2	3.8	7.0	841	40	4.8	3.4	6.4	837	13	1.6	0.8	2.6
		18-35M	802	40	5.0	3.6	6.7	802	35	4.4	3.1	6.0	802	6	0.7	0.3	1.6
Overall/subject	Q-QIV	6-17M	481	53	11.0	8.4	14.2	481	45	9.4	6.9	12.3	481	15	3.1	1.8	5.1
		18-35M	678	56	8.3	6.3	10.6	678	41	6.0	4.4	8.1	675	19	2.8	1.7	4.4
	F-QIV	6-17M	470	41	8.7	6.3	11.6	470	37	7.9	5.6	10.7	469	13	2.8	1.5	4.7
		18-35M	682	38	5.6	4.0	7.6	682	33	4.8	3.4	6.7	682	6	0.9	0.3	1.9

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 100 Incidence of solicited local AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total vaccinated cohort)

		Q-QIV										F-QIV									
		6-17M					18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																					
Pain	All	478	175	36.6	32.3	41.1	673	289	42.9	39.2	46.8	465	173	37.2	32.8	41.8	681	256	37.6	33.9	41.4
	Grade 2 or 3	478	52	10.9	8.2	14.0	673	98	14.6	12.0	17.5	465	48	10.3	7.7	13.5	681	79	11.6	9.3	14.2
	Grade 3	478	11	2.3	1.2	4.1	673	17	2.5	1.5	4.0	465	12	2.6	1.3	4.5	681	4	0.6	0.2	1.5
	Medical advice	478	0	0.0	0.0	0.8	673	0	0.0	0.0	0.5	465	2	0.4	0.1	1.5	681	1	0.1	0.0	0.8
Redness (mm)	All	478	2	0.4	0.1	1.5	673	13	1.9	1.0	3.3	465	2	0.4	0.1	1.5	681	13	1.9	1.0	3.2
	>50	478	0	0.0	0.0	0.8	673	5	0.7	0.2	1.7	465	0	0.0	0.0	0.8	681	4	0.6	0.2	1.5
	>100	478	0	0.0	0.0	0.8	673	0	0.0	0.0	0.5	465	0	0.0	0.0	0.8	681	0	0.0	0.0	0.5
	Medical advice	478	0	0.0	0.0	0.8	673	0	0.0	0.0	0.5	465	0	0.0	0.0	0.8	681	2	0.3	0.0	1.1
Swelling (mm)	All	478	4	0.8	0.2	2.1	673	7	1.0	0.4	2.1	465	0	0.0	0.0	0.8	681	5	0.7	0.2	1.7
	>50	478	1	0.2	0.0	1.2	673	1	0.1	0.0	0.8	465	0	0.0	0.0	0.8	681	0	0.0	0.0	0.5
	>100	478	0	0.0	0.0	0.8	673	0	0.0	0.0	0.5	465	0	0.0	0.0	0.8	681	0	0.0	0.0	0.5
	Medical advice	478	0	0.0	0.0	0.8	673	0	0.0	0.0	0.5	465	0	0.0	0.0	0.8	681	0	0.0	0.0	0.5
Dose 2																					
Pain	All	373	103	27.6	23.1	32.5	117	35	29.9	21.8	39.1	372	108	29.0	24.5	33.9	121	39	32.2	24.0	41.3
	Grade 2 or 3	373	20	5.4	3.3	8.2	117	11	9.4	4.8	16.2	372	26	7.0	4.6	10.1	121	10	8.3	4.0	14.7
	Grade 3	373	6	1.6	0.6	3.5	117	3	2.6	0.5	7.3	372	1	0.3	0.0	1.5	121	2	1.7	0.2	5.8
	Medical advice	373	0	0.0	0.0	1.0	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
Redness (mm)	All	373	1	0.3	0.0	1.5	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	2	1.7	0.2	5.8
	>50	373	0	0.0	0.0	1.0	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	>100	373	0	0.0	0.0	1.0	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	Medical advice	373	1	0.3	0.0	1.5	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
Swelling (mm)	All	373	0	0.0	0.0	1.0	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	>50	373	0	0.0	0.0	1.0	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	>100	373	0	0.0	0.0	1.0	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	Medical advice	373	0	0.0	0.0	1.0	117	0	0.0	0.0	3.1	372	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
Overall/dose																					
Pain	All	851	278	32.7	29.5	35.9	790	324	41.0	37.6	44.5	837	281	33.6	30.4	36.9	802	295	36.8	33.4	40.2
	Grade 2 or 3	851	72	8.5	6.7	10.5	790	109	13.8	11.5	16.4	837	74	8.8	7.0	11.0	802	89	11.1	9.0	13.5
	Grade 3	851	17	2.0	1.2	3.2	790	20	2.5	1.6	3.9	837	13	1.6	0.8	2.6	802	6	0.7	0.3	1.6
	Medical advice	851	0	0.0	0.0	0.4	790	0	0.0	0.0	0.5	837	2	0.2	0.0	0.9	802	1	0.1	0.0	0.7

		Q-QIV										F-QIV									
		6-17M					18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Redness (mm)	All	851	3	0.4	0.1	1.0	790	13	1.6	0.9	2.8	837	2	0.2	0.0	0.9	802	15	1.9	1.1	3.1
	>50	851	0	0.0	0.0	0.4	790	5	0.6	0.2	1.5	837	0	0.0	0.0	0.4	802	4	0.5	0.1	1.3
	>100	851	0	0.0	0.0	0.4	790	0	0.0	0.0	0.5	837	0	0.0	0.0	0.4	802	0	0.0	0.0	0.5
	Medical advice	851	1	0.1	0.0	0.7	790	0	0.0	0.0	0.5	837	0	0.0	0.0	0.4	802	2	0.2	0.0	0.9
Swelling (mm)	All	851	4	0.5	0.1	1.2	790	7	0.9	0.4	1.8	837	0	0.0	0.0	0.4	802	5	0.6	0.2	1.4
	>50	851	1	0.1	0.0	0.7	790	1	0.1	0.0	0.7	837	0	0.0	0.0	0.4	802	0	0.0	0.0	0.5
	>100	851	0	0.0	0.0	0.4	790	0	0.0	0.0	0.5	837	0	0.0	0.0	0.4	802	0	0.0	0.0	0.5
	Medical advice	851	0	0.0	0.0	0.4	790	0	0.0	0.0	0.5	837	0	0.0	0.0	0.4	802	0	0.0	0.0	0.5
Overall/subject																					
Pain	All	481	211	43.9	39.4	48.4	675	298	44.1	40.4	48.0	469	196	41.8	37.3	46.4	682	266	39.0	35.3	42.8
	Grade 2 or 3	481	61	12.7	9.8	16.0	675	103	15.3	12.6	18.2	469	66	14.1	11.1	17.6	682	84	12.3	9.9	15.0
	Grade 3	481	15	3.1	1.8	5.1	675	19	2.8	1.7	4.4	469	13	2.8	1.5	4.7	682	6	0.9	0.3	1.9
	Medical advice	481	0	0.0	0.0	0.8	675	0	0.0	0.0	0.5	469	2	0.4	0.1	1.5	682	1	0.1	0.0	0.8
Redness (mm)	All	481	3	0.6	0.1	1.8	675	13	1.9	1.0	3.3	469	2	0.4	0.1	1.5	682	14	2.1	1.1	3.4
	>50	481	0	0.0	0.0	0.8	675	5	0.7	0.2	1.7	469	0	0.0	0.0	0.8	682	4	0.6	0.2	1.5
	>100	481	0	0.0	0.0	0.8	675	0	0.0	0.0	0.5	469	0	0.0	0.0	0.8	682	0	0.0	0.0	0.5
	Medical advice	481	1	0.2	0.0	1.2	675	0	0.0	0.0	0.5	469	0	0.0	0.0	0.8	682	2	0.3	0.0	1.1
Swelling (mm)	All	481	4	0.8	0.2	2.1	675	7	1.0	0.4	2.1	469	0	0.0	0.0	0.8	682	5	0.7	0.2	1.7
	>50	481	1	0.2	0.0	1.2	675	1	0.1	0.0	0.8	469	0	0.0	0.0	0.8	682	0	0.0	0.0	0.5
	>100	481	0	0.0	0.0	0.8	675	0	0.0	0.0	0.5	469	0	0.0	0.0	0.8	682	0	0.0	0.0	0.5
	Medical advice	481	0	0.0	0.0	0.8	675	0	0.0	0.0	0.5	469	0	0.0	0.0	0.8	682	0	0.0	0.0	0.5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 101 Incidence of solicited general AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by age strata (Total vaccinated cohort)

		Q-QIV										F-QIV									
		6-17M					18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1																					
Drowsiness	All	478	200	41.8	37.4	46.4	677	224	33.1	29.5	36.8	467	210	45.0	40.4	49.6	681	214	31.4	28.0	35.1
	Grade 2 or 3	478	62	13.0	10.1	16.3	677	70	10.3	8.1	12.9	467	76	16.3	13.0	19.9	681	67	9.8	7.7	12.3
	Grade 3	478	16	3.3	1.9	5.4	677	15	2.2	1.2	3.6	467	17	3.6	2.1	5.8	681	13	1.9	1.0	3.2
	Related	478	171	35.8	31.5	40.3	677	194	28.7	25.3	32.2	467	189	40.5	36.0	45.1	681	192	28.2	24.8	31.7
	Grade 3 Related	478	14	2.9	1.6	4.9	677	13	1.9	1.0	3.3	467	16	3.4	2.0	5.5	681	12	1.8	0.9	3.1
	Medical advice	478	6	1.3	0.5	2.7	677	6	0.9	0.3	1.9	467	3	0.6	0.1	1.9	681	4	0.6	0.2	1.5
Fever/(Axillary) (°C)	All	478	80	16.7	13.5	20.4	677	66	9.7	7.6	12.2	467	70	15.0	11.9	18.6	681	77	11.3	9.0	13.9
	≥38	478	40	8.4	6.0	11.2	677	25	3.7	2.4	5.4	467	31	6.6	4.6	9.3	681	36	5.3	3.7	7.2
	>38.5	478	25	5.2	3.4	7.6	677	8	1.2	0.5	2.3	467	15	3.2	1.8	5.2	681	15	2.2	1.2	3.6
	>39.0	478	12	2.5	1.3	4.3	677	4	0.6	0.2	1.5	467	4	0.9	0.2	2.2	681	7	1.0	0.4	2.1
	>39.5	478	9	1.9	0.9	3.5	677	2	0.3	0.0	1.1	467	2	0.4	0.1	1.5	681	2	0.3	0.0	1.1
	>40.0	478	2	0.4	0.1	1.5	677	0	0.0	0.0	0.5	467	0	0.0	0.0	0.8	681	0	0.0	0.0	0.5
	Related	478	25	5.2	3.4	7.6	677	16	2.4	1.4	3.8	467	26	5.6	3.7	8.1	681	24	3.5	2.3	5.2
	≥38 Related	478	25	5.2	3.4	7.6	677	16	2.4	1.4	3.8	467	26	5.6	3.7	8.1	681	24	3.5	2.3	5.2
	>38.5 Related	478	13	2.7	1.5	4.6	677	3	0.4	0.1	1.3	467	13	2.8	1.5	4.7	681	6	0.9	0.3	1.9
	>39.0 Related	478	6	1.3	0.5	2.7	677	2	0.3	0.0	1.1	467	4	0.9	0.2	2.2	681	2	0.3	0.0	1.1
	>39.5 Related	478	4	0.8	0.2	2.1	677	0	0.0	0.0	0.5	467	2	0.4	0.1	1.5	681	1	0.1	0.0	0.8
	>40.0 Related	478	0	0.0	0.0	0.8	677	0	0.0	0.0	0.5	467	0	0.0	0.0	0.8	681	0	0.0	0.0	0.5
	Medical advice	478	11	2.3	1.2	4.1	677	6	0.9	0.3	1.9	467	4	0.9	0.2	2.2	681	6	0.9	0.3	1.9
Irritability / Fussiness	All	478	273	57.1	52.5	61.6	677	297	43.9	40.1	47.7	467	252	54.0	49.3	58.6	681	275	40.4	36.7	44.2
	Grade 2 or 3	478	110	23.0	19.3	27.1	677	114	16.8	14.1	19.9	467	97	20.8	17.2	24.7	681	95	14.0	11.4	16.8
	Grade 3	478	24	5.0	3.2	7.4	677	20	3.0	1.8	4.5	467	15	3.2	1.8	5.2	681	19	2.8	1.7	4.3
	Related	478	239	50.0	45.4	54.6	677	260	38.4	34.7	42.2	467	227	48.6	44.0	53.2	681	246	36.1	32.5	39.9
	Grade 3 Related	478	20	4.2	2.6	6.4	677	17	2.5	1.5	4.0	467	15	3.2	1.8	5.2	681	18	2.6	1.6	4.1
	Medical advice	478	9	1.9	0.9	3.5	677	8	1.2	0.5	2.3	467	3	0.6	0.1	1.9	681	9	1.3	0.6	2.5
Loss Of Appetite	All	478	141	29.5	25.4	33.8	677	193	28.5	25.1	32.1	467	131	28.1	24.0	32.4	681	197	28.9	25.5	32.5
	Grade 2 or 3	478	35	7.3	5.2	10.0	677	48	7.1	5.3	9.3	467	40	8.6	6.2	11.5	681	52	7.6	5.8	9.9

		Q-QIV										F-QIV									
		6-17M					18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI				95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3	478	7	1.5	0.6	3.0	677	12	1.8	0.9	3.1	467	4	0.9	0.2	2.2	681	11	1.6	0.8	2.9
	Related	478	122	25.5	21.7	29.7	677	158	23.3	20.2	26.7	467	115	24.6	20.8	28.8	681	175	25.7	22.5	29.2
	Grade 3 Related	478	6	1.3	0.5	2.7	677	10	1.5	0.7	2.7	467	4	0.9	0.2	2.2	681	10	1.5	0.7	2.7
	Medical advice	478	6	1.3	0.5	2.7	677	8	1.2	0.5	2.3	467	2	0.4	0.1	1.5	681	7	1.0	0.4	2.1
Dose 2																					
Drowsiness	All	373	129	34.6	29.8	39.7	117	28	23.9	16.5	32.7	374	142	38.0	33.0	43.1	121	24	19.8	13.1	28.1
	Grade 2 or 3	373	37	9.9	7.1	13.4	117	6	5.1	1.9	10.8	374	45	12.0	8.9	15.8	121	8	6.6	2.9	12.6
	Grade 3	373	10	2.7	1.3	4.9	117	0	0.0	0.0	3.1	374	6	1.6	0.6	3.5	121	0	0.0	0.0	3.0
	Related	373	111	29.8	25.2	34.7	117	22	18.8	12.2	27.1	374	115	30.7	26.1	35.7	121	21	17.4	11.1	25.3
	Grade 3 Related	373	6	1.6	0.6	3.5	117	0	0.0	0.0	3.1	374	2	0.5	0.1	1.9	121	0	0.0	0.0	3.0
	Medical advice	373	3	0.8	0.2	2.3	117	2	1.7	0.2	6.0	374	5	1.3	0.4	3.1	121	1	0.8	0.0	4.5
Fever/(Axillary) (°C)	All	373	47	12.6	9.4	16.4	117	13	11.1	6.1	18.3	374	38	10.2	7.3	13.7	121	10	8.3	4.0	14.7
	≥38	373	23	6.2	3.9	9.1	117	8	6.8	3.0	13.0	374	16	4.3	2.5	6.9	121	6	5.0	1.8	10.5
	>38.5	373	11	2.9	1.5	5.2	117	6	5.1	1.9	10.8	374	6	1.6	0.6	3.5	121	5	4.1	1.4	9.4
	>39.0	373	5	1.3	0.4	3.1	117	4	3.4	0.9	8.5	374	3	0.8	0.2	2.3	121	3	2.5	0.5	7.1
	>39.5	373	3	0.8	0.2	2.3	117	1	0.9	0.0	4.7	374	0	0.0	0.0	1.0	121	1	0.8	0.0	4.5
	>40.0	373	3	0.8	0.2	2.3	117	0	0.0	0.0	3.1	374	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	Related	373	17	4.6	2.7	7.2	117	5	4.3	1.4	9.7	374	11	2.9	1.5	5.2	121	3	2.5	0.5	7.1
	≥38 Related	373	15	4.0	2.3	6.5	117	5	4.3	1.4	9.7	374	10	2.7	1.3	4.9	121	3	2.5	0.5	7.1
	>38.5 Related	373	7	1.9	0.8	3.8	117	5	4.3	1.4	9.7	374	3	0.8	0.2	2.3	121	2	1.7	0.2	5.8
	>39.0 Related	373	2	0.5	0.1	1.9	117	4	3.4	0.9	8.5	374	1	0.3	0.0	1.5	121	1	0.8	0.0	4.5
	>39.5 Related	373	1	0.3	0.0	1.5	117	1	0.9	0.0	4.7	374	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	>40.0 Related	373	1	0.3	0.0	1.5	117	0	0.0	0.0	3.1	374	0	0.0	0.0	1.0	121	0	0.0	0.0	3.0
	Medical advice	373	6	1.6	0.6	3.5	117	3	2.6	0.5	7.3	374	6	1.6	0.6	3.5	121	1	0.8	0.0	4.5
Irritability / Fussiness	All	373	168	45.0	39.9	50.2	117	43	36.8	28.0	46.2	374	177	47.3	42.2	52.5	121	37	30.6	22.5	39.6
	Grade 2 or 3	373	60	16.1	12.5	20.2	117	15	12.8	7.4	20.3	374	61	16.3	12.7	20.5	121	10	8.3	4.0	14.7
	Grade 3	373	16	4.3	2.5	6.9	117	5	4.3	1.4	9.7	374	12	3.2	1.7	5.5	121	2	1.7	0.2	5.8
	Related	373	150	40.2	35.2	45.4	117	35	29.9	21.8	39.1	374	141	37.7	32.8	42.8	121	34	28.1	20.3	37.0
	Grade 3 Related	373	13	3.5	1.9	5.9	117	5	4.3	1.4	9.7	374	7	1.9	0.8	3.8	121	2	1.7	0.2	5.8
	Medical advice	373	5	1.3	0.4	3.1	117	2	1.7	0.2	6.0	374	11	2.9	1.5	5.2	121	0	0.0	0.0	3.0

		Q-QIV										F-QIV									
		6-17M					18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI				95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Loss Of Appetite	All	373	90	24.1	19.9	28.8	117	20	17.1	10.8	25.2	374	91	24.3	20.1	29.0	121	25	20.7	13.8	29.0
	Grade 2 or 3	373	29	7.8	5.3	11.0	117	3	2.6	0.5	7.3	374	23	6.1	3.9	9.1	121	6	5.0	1.8	10.5
	Grade 3	373	8	2.1	0.9	4.2	117	0	0.0	0.0	3.1	374	3	0.8	0.2	2.3	121	2	1.7	0.2	5.8
	Related	373	73	19.6	15.7	24.0	117	18	15.4	9.4	23.2	374	66	17.6	13.9	21.9	121	21	17.4	11.1	25.3
	Grade 3 Related	373	4	1.1	0.3	2.7	117	0	0.0	0.0	3.1	374	1	0.3	0.0	1.5	121	1	0.8	0.0	4.5
	Medical advice	373	4	1.1	0.3	2.7	117	1	0.9	0.0	4.7	374	10	2.7	1.3	4.9	121	1	0.8	0.0	4.5
Overall/dose																					
Drowsiness	All	851	329	38.7	35.4	42.0	794	252	31.7	28.5	35.1	841	352	41.9	38.5	45.3	802	238	29.7	26.5	33.0
	Grade 2 or 3	851	99	11.6	9.6	14.0	794	76	9.6	7.6	11.8	841	121	14.4	12.1	16.9	802	75	9.4	7.4	11.6
	Grade 3	851	26	3.1	2.0	4.4	794	15	1.9	1.1	3.1	841	23	2.7	1.7	4.1	802	13	1.6	0.9	2.8
	Related	851	282	33.1	30.0	36.4	794	216	27.2	24.1	30.4	841	304	36.1	32.9	39.5	802	213	26.6	23.5	29.8
	Grade 3 Related	851	20	2.4	1.4	3.6	794	13	1.6	0.9	2.8	841	18	2.1	1.3	3.4	802	12	1.5	0.8	2.6
	Medical advice	851	9	1.1	0.5	2.0	794	8	1.0	0.4	2.0	841	8	1.0	0.4	1.9	802	5	0.6	0.2	1.4
Fever/(Axillary) (°C)	All	851	127	14.9	12.6	17.5	794	79	9.9	8.0	12.2	841	108	12.8	10.7	15.3	802	87	10.8	8.8	13.2
	≥38	851	63	7.4	5.7	9.4	794	33	4.2	2.9	5.8	841	47	5.6	4.1	7.4	802	42	5.2	3.8	7.0
	>38.5	851	36	4.2	3.0	5.8	794	14	1.8	1.0	2.9	841	21	2.5	1.6	3.8	802	20	2.5	1.5	3.8
	>39.0	851	17	2.0	1.2	3.2	794	8	1.0	0.4	2.0	841	7	0.8	0.3	1.7	802	10	1.2	0.6	2.3
	>39.5	851	12	1.4	0.7	2.5	794	3	0.4	0.1	1.1	841	2	0.2	0.0	0.9	802	3	0.4	0.1	1.1
	>40.0	851	5	0.6	0.2	1.4	794	0	0.0	0.0	0.5	841	0	0.0	0.0	0.4	802	0	0.0	0.0	0.5
	Related	851	42	4.9	3.6	6.6	794	21	2.6	1.6	4.0	841	37	4.4	3.1	6.0	802	27	3.4	2.2	4.9
	≥38 Related	851	40	4.7	3.4	6.3	794	21	2.6	1.6	4.0	841	36	4.3	3.0	5.9	802	27	3.4	2.2	4.9
	>38.5 Related	851	20	2.4	1.4	3.6	794	8	1.0	0.4	2.0	841	16	1.9	1.1	3.1	802	8	1.0	0.4	2.0
	>39.0 Related	851	8	0.9	0.4	1.8	794	6	0.8	0.3	1.6	841	5	0.6	0.2	1.4	802	3	0.4	0.1	1.1
	>39.5 Related	851	5	0.6	0.2	1.4	794	1	0.1	0.0	0.7	841	2	0.2	0.0	0.9	802	1	0.1	0.0	0.7
	>40.0 Related	851	1	0.1	0.0	0.7	794	0	0.0	0.0	0.5	841	0	0.0	0.0	0.4	802	0	0.0	0.0	0.5
	Medical advice	851	17	2.0	1.2	3.2	794	9	1.1	0.5	2.1	841	10	1.2	0.6	2.2	802	7	0.9	0.4	1.8
Irritability / Fussiness	All	851	441	51.8	48.4	55.2	794	340	42.8	39.3	46.3	841	429	51.0	47.6	54.4	802	312	38.9	35.5	42.4
	Grade 2 or 3	851	170	20.0	17.3	22.8	794	129	16.2	13.7	19.0	841	158	18.8	16.2	21.6	802	105	13.1	10.8	15.6
	Grade 3	851	40	4.7	3.4	6.3	794	25	3.1	2.0	4.6	841	27	3.2	2.1	4.6	802	21	2.6	1.6	4.0
	Related	851	389	45.7	42.3	49.1	794	295	37.2	33.8	40.6	841	368	43.8	40.4	47.2	802	280	34.9	31.6	38.3

		Q-QIV										F-QIV									
		6-17M					18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3 Related	851	33	3.9	2.7	5.4	794	22	2.8	1.7	4.2	841	22	2.6	1.6	3.9	802	20	2.5	1.5	3.8
	Medical advice	851	14	1.6	0.9	2.7	794	10	1.3	0.6	2.3	841	14	1.7	0.9	2.8	802	9	1.1	0.5	2.1
Loss Of Appetite	All	851	231	27.1	24.2	30.3	794	213	26.8	23.8	30.1	841	222	26.4	23.4	29.5	802	222	27.7	24.6	30.9
	Grade 2 or 3	851	64	7.5	5.8	9.5	794	51	6.4	4.8	8.4	841	63	7.5	5.8	9.5	802	58	7.2	5.5	9.2
	Grade 3	851	15	1.8	1.0	2.9	794	12	1.5	0.8	2.6	841	7	0.8	0.3	1.7	802	13	1.6	0.9	2.8
	Related	851	195	22.9	20.1	25.9	794	176	22.2	19.3	25.2	841	181	21.5	18.8	24.5	802	196	24.4	21.5	27.6
	Grade 3 Related	851	10	1.2	0.6	2.2	794	10	1.3	0.6	2.3	841	5	0.6	0.2	1.4	802	11	1.4	0.7	2.4
	Medical advice	851	10	1.2	0.6	2.2	794	9	1.1	0.5	2.1	841	12	1.4	0.7	2.5	802	8	1.0	0.4	2.0
Overall/subject																					
Drowsiness	All	481	238	49.5	44.9	54.0	678	233	34.4	30.8	38.1	470	248	52.8	48.1	57.4	682	223	32.7	29.2	36.4
	Grade 2 or 3	481	85	17.7	14.4	21.4	678	75	11.1	8.8	13.7	470	104	22.1	18.5	26.2	682	73	10.7	8.5	13.3
	Grade 3	481	21	4.4	2.7	6.6	678	15	2.2	1.2	3.6	470	21	4.5	2.8	6.7	682	13	1.9	1.0	3.2
	Related	481	209	43.5	39.0	48.0	678	202	29.8	26.4	33.4	470	224	47.7	43.1	52.3	682	201	29.5	26.1	33.1
	Grade 3 Related	481	16	3.3	1.9	5.3	678	13	1.9	1.0	3.3	470	17	3.6	2.1	5.7	682	12	1.8	0.9	3.1
	Medical advice	481	8	1.7	0.7	3.3	678	7	1.0	0.4	2.1	470	8	1.7	0.7	3.3	682	5	0.7	0.2	1.7
Fever/(Axillary) (°C)	All	481	109	22.7	19.0	26.7	678	74	10.9	8.7	13.5	470	93	19.8	16.3	23.7	682	85	12.5	10.1	15.2
	≥38	481	60	12.5	9.7	15.8	678	31	4.6	3.1	6.4	470	45	9.6	7.1	12.6	682	41	6.0	4.3	8.1
	>38.5	481	35	7.3	5.1	10.0	678	13	1.9	1.0	3.3	470	21	4.5	2.8	6.7	682	20	2.9	1.8	4.5
	>39.0	481	17	3.5	2.1	5.6	678	8	1.2	0.5	2.3	470	7	1.5	0.6	3.0	682	10	1.5	0.7	2.7
	>39.5	481	12	2.5	1.3	4.3	678	3	0.4	0.1	1.3	470	2	0.4	0.1	1.5	682	3	0.4	0.1	1.3
	>40.0	481	5	1.0	0.3	2.4	678	0	0.0	0.0	0.5	470	0	0.0	0.0	0.8	682	0	0.0	0.0	0.5
	Related	481	41	8.5	6.2	11.4	678	21	3.1	1.9	4.7	470	36	7.7	5.4	10.4	682	27	4.0	2.6	5.7
	≥38 Related	481	39	8.1	5.8	10.9	678	21	3.1	1.9	4.7	470	35	7.4	5.2	10.2	682	27	4.0	2.6	5.7
	>38.5 Related	481	20	4.2	2.6	6.3	678	8	1.2	0.5	2.3	470	16	3.4	2.0	5.5	682	8	1.2	0.5	2.3
	>39.0 Related	481	8	1.7	0.7	3.3	678	6	0.9	0.3	1.9	470	5	1.1	0.3	2.5	682	3	0.4	0.1	1.3
	>39.5 Related	481	5	1.0	0.3	2.4	678	1	0.1	0.0	0.8	470	2	0.4	0.1	1.5	682	1	0.1	0.0	0.8
	>40.0 Related	481	1	0.2	0.0	1.2	678	0	0.0	0.0	0.5	470	0	0.0	0.0	0.8	682	0	0.0	0.0	0.5
	Medical advice	481	16	3.3	1.9	5.3	678	8	1.2	0.5	2.3	470	10	2.1	1.0	3.9	682	7	1.0	0.4	2.1
Irritability / Fussiness	All	481	315	65.5	61.1	69.7	678	315	46.5	42.7	50.3	470	297	63.2	58.7	67.6	682	285	41.8	38.1	45.6
	Grade 2 or 3	481	144	29.9	25.9	34.2	678	121	17.8	15.0	20.9	470	128	27.2	23.3	31.5	682	101	14.8	12.2	17.7

		Q-QIV										F-QIV									
		6-17M					18-35M					6-17M					18-35M				
					95 % CI					95 % CI					95 % CI				95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3	481	36	7.5	5.3	10.2	678	25	3.7	2.4	5.4	470	25	5.3	3.5	7.8	682	20	2.9	1.8	4.5
	Related	481	280	58.2	53.7	62.7	678	278	41.0	37.3	44.8	470	269	57.2	52.6	61.8	682	256	37.5	33.9	41.3
	Grade 3 Related	481	30	6.2	4.2	8.8	678	22	3.2	2.0	4.9	470	20	4.3	2.6	6.5	682	19	2.8	1.7	4.3
	Medical advice	481	13	2.7	1.4	4.6	678	10	1.5	0.7	2.7	470	13	2.8	1.5	4.7	682	9	1.3	0.6	2.5
Loss Of Appetite	All	481	188	39.1	34.7	43.6	678	203	29.9	26.5	33.5	470	175	37.2	32.8	41.8	682	210	30.8	27.3	34.4
	Grade 2 or 3	481	59	12.3	9.5	15.5	678	50	7.4	5.5	9.6	470	56	11.9	9.1	15.2	682	56	8.2	6.3	10.5
	Grade 3	481	14	2.9	1.6	4.8	678	12	1.8	0.9	3.1	470	6	1.3	0.5	2.8	682	13	1.9	1.0	3.2
	Related	481	159	33.1	28.9	37.5	678	169	24.9	21.7	28.4	470	148	31.5	27.3	35.9	682	189	27.7	24.4	31.2
	Grade 3 Related	481	9	1.9	0.9	3.5	678	10	1.5	0.7	2.7	470	5	1.1	0.3	2.5	682	11	1.6	0.8	2.9
	Medical advice	481	9	1.9	0.9	3.5	678	8	1.2	0.5	2.3	470	11	2.3	1.2	4.1	682	8	1.2	0.5	2.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 102 Number of days with solicited local and general AEs during the 7-day follow-up period by age strata (Total vaccinated cohort)

Solicited symptom	Dose	Group	Sub-group	N	Mean	Min	Q1	Median	Q3	Max
Drowsiness	Dose 1	Q-QIV	6-17M	200	2.1	1.0	1.0	2.0	2.0	7.0
			18-35M	224	1.9	1.0	1.0	1.0	2.0	7.0
		F-QIV	6-17M	210	2.1	1.0	1.0	2.0	3.0	7.0
			18-35M	214	1.9	1.0	1.0	1.0	2.0	7.0
	Dose 2	Q-QIV	6-17M	129	2.0	1.0	1.0	2.0	2.0	7.0
			18-35M	28	2.1	1.0	1.0	2.0	2.0	7.0
		F-QIV	6-17M	142	2.2	1.0	1.0	2.0	3.0	7.0
			18-35M	24	1.7	1.0	1.0	1.0	2.0	4.0
	Overall/dose	Q-QIV	6-17M	329	2.1	1.0	1.0	2.0	2.0	7.0
			18-35M	252	1.9	1.0	1.0	1.0	2.0	7.0
		F-QIV	6-17M	352	2.1	1.0	1.0	2.0	3.0	7.0
			18-35M	238	1.9	1.0	1.0	1.0	2.0	7.0
Irritability / fussiness	Dose 1	Q-QIV	6-17M	273	2.4	1.0	1.0	2.0	3.0	7.0
			18-35M	297	2.3	1.0	1.0	2.0	3.0	7.0
		F-QIV	6-17M	252	2.6	1.0	1.0	2.0	3.0	7.0
			18-35M	275	2.4	1.0	1.0	2.0	3.0	7.0
	Dose 2	Q-QIV	6-17M	168	2.5	1.0	1.0	2.0	3.0	7.0
			18-35M	43	2.5	1.0	1.0	2.0	3.0	7.0
		F-QIV	6-17M	177	2.4	1.0	1.0	2.0	3.0	7.0
			18-35M	37	2.0	1.0	1.0	1.0	2.0	7.0
	Overall/dose	Q-QIV	6-17M	441	2.5	1.0	1.0	2.0	3.0	7.0
			18-35M	340	2.3	1.0	1.0	2.0	3.0	7.0
		F-QIV	6-17M	429	2.5	1.0	1.0	2.0	3.0	7.0
			18-35M	312	2.3	1.0	1.0	2.0	3.0	7.0
Loss of appetite	Dose 1	Q-QIV	6-17M	141	2.3	1.0	1.0	2.0	3.0	7.0
			18-35M	193	2.2	1.0	1.0	2.0	3.0	7.0
		F-QIV	6-17M	131	2.3	1.0	1.0	2.0	3.0	7.0
			18-35M	197	2.3	1.0	1.0	2.0	3.0	7.0
	Dose 2	Q-QIV	6-17M	90	2.5	1.0	1.0	2.0	3.0	7.0
			18-35M	20	2.6	1.0	1.0	2.0	2.5	7.0
		F-QIV	6-17M	91	2.2	1.0	1.0	2.0	3.0	7.0
			18-35M	25	2.4	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	6-17M	231	2.4	1.0	1.0	2.0	3.0	7.0
			18-35M	213	2.2	1.0	1.0	2.0	3.0	7.0
		F-QIV	6-17M	222	2.2	1.0	1.0	2.0	3.0	7.0
			18-35M	222	2.3	1.0	1.0	2.0	3.0	7.0
Pain	Dose 1	Q-QIV	6-17M	175	1.7	1.0	1.0	1.0	2.0	7.0
			18-35M	289	1.9	1.0	1.0	2.0	2.0	7.0
		F-QIV	6-17M	173	1.8	1.0	1.0	1.0	2.0	6.0
			18-35M	256	1.9	1.0	1.0	2.0	2.0	6.0
	Dose 2	Q-QIV	6-17M	103	1.7	1.0	1.0	1.0	2.0	6.0
			18-35M	35	1.7	1.0	1.0	1.0	2.0	5.0
		F-QIV	6-17M	108	1.8	1.0	1.0	2.0	2.0	5.0
			18-35M	39	1.5	1.0	1.0	1.0	2.0	4.0
	Overall/dose	Q-QIV	6-17M	278	1.7	1.0	1.0	1.0	2.0	7.0
			18-35M	324	1.8	1.0	1.0	2.0	2.0	7.0
		F-QIV	6-17M	281	1.8	1.0	1.0	1.0	2.0	6.0
			18-35M	295	1.8	1.0	1.0	2.0	2.0	6.0
Redness	Dose 1	Q-QIV	6-17M	2	1.5	1.0	1.0	1.5	2.0	2.0
			18-35M	13	2.1	1.0	1.0	2.0	3.0	4.0
		F-QIV	6-17M	2	1.0	1.0	1.0	1.0	1.0	1.0
			18-35M	13	2.2	1.0	1.0	1.0	3.0	6.0

Solicited symptom	Dose	Group	Sub-group	N	Mean	Min	Q1	Median	Q3	Max
	Dose 2	Q-QIV	6-17M	1	1.0	1.0	1.0	1.0	1.0	1.0
		F-QIV	18-35M	2	1.5	1.0	1.0	1.5	2.0	2.0
	Overall/dose	Q-QIV	6-17M	3	1.3	1.0	1.0	1.0	2.0	2.0
			18-35M	13	2.1	1.0	1.0	2.0	3.0	4.0
		F-QIV	6-17M	2	1.0	1.0	1.0	1.0	1.0	1.0
			18-35M	15	2.1	1.0	1.0	1.0	3.0	6.0
Swelling	Dose 1	Q-QIV	6-17M	4	1.5	1.0	1.0	1.5	2.0	2.0
			18-35M	7	2.9	1.0	2.0	2.0	5.0	5.0
		F-QIV	18-35M	5	1.8	1.0	1.0	2.0	2.0	3.0
	Overall/dose	Q-QIV	6-17M	4	1.5	1.0	1.0	1.5	2.0	2.0
			18-35M	7	2.9	1.0	2.0	2.0	5.0	5.0
		F-QIV	18-35M	5	1.8	1.0	1.0	2.0	2.0	3.0
Fever	Dose 1	Q-QIV	6-17M	80	2.2	1.0	1.0	2.0	3.0	7.0
			18-35M	66	1.8	1.0	1.0	1.0	2.0	6.0
		F-QIV	6-17M	70	2.0	1.0	1.0	1.0	3.0	7.0
			18-35M	77	1.7	1.0	1.0	1.0	2.0	6.0
	Dose 2	Q-QIV	6-17M	47	1.8	1.0	1.0	1.0	2.0	7.0
			18-35M	13	1.5	1.0	1.0	1.0	2.0	3.0
		F-QIV	6-17M	38	2.2	1.0	1.0	1.5	3.0	7.0
			18-35M	10	1.7	1.0	1.0	2.0	2.0	3.0
	Overall/dose	Q-QIV	6-17M	127	2.1	1.0	1.0	2.0	2.0	7.0
			18-35M	79	1.7	1.0	1.0	1.0	2.0	6.0
		F-QIV	6-17M	108	2.1	1.0	1.0	1.0	3.0	7.0
			18-35M	87	1.7	1.0	1.0	1.0	2.0	6.0

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
N = number of doses with the symptom
Q1 = 25th percentile
Q3 = 75th percentile

Table 103 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		268	53.6	49.1	58.0	281	39.7	36.1	43.5	270	53.8	49.3	58.2	267	37.3	33.8	41.0
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Iron deficiency anaemia (10022972)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Leukocytosis (10024378)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Lymphadenopathy (10025197)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Neutropenia (10029354)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Congenital, familial and genetic disorders (10010331)	Phimosis (10034878)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Tibial torsion (10064515)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	4	0.8	0.2	2.0	1	0.1	0.0	0.8
	Ear discomfort (10052137)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Ear pain (10014020)	2	0.4	0.0	1.4	4	0.6	0.2	1.4	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Middle ear effusion (10062545)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dacryostenosis acquired (10053990)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Eye discharge (10015915)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Eye pruritus (10052140)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Eyelid oedema (10015993)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Lacrimation increased (10023644)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Photophobia (10034960)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Gastrointestinal disorders (10017947)	Abdominal discomfort (10000059)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Abdominal hernia (10060954)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Abdominal pain upper (10000087)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Constipation (10010774)	4	0.8	0.2	2.0	1	0.1	0.0	0.8	5	1.0	0.3	2.3	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Dental caries (10012318)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Diarrhoea (10012735)	27	5.4	3.6	7.8	39	5.5	4.0	7.5	23	4.6	2.9	6.8	30	4.2	2.8	5.9
	Faeces hard (10016101)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Flatulence (10016766)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Food poisoning (10016952)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Frequent bowel movements (10017367)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Haematochezia (10018836)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Nausea (10028813)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Regurgitation (10067171)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Stomatitis (10042128)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Teething (10043183)	13	2.6	1.4	4.4	2	0.3	0.0	1.0	19	3.8	2.3	5.8	2	0.3	0.0	1.0
	Vomiting (10047700)	25	5.0	3.3	7.3	22	3.1	2.0	4.7	20	4.0	2.5	6.1	26	3.6	2.4	5.3
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Administration site rash (10071156)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Asthenia (10003549)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Chills (10008531)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Developmental delay (10012559)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Discomfort (10013082)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Fatigue (10016256)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Feeling hot (10016334)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Ill-defined disorder (10061520)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Influenza like illness (10022004)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Injection site bruising (10022052)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Injection site pruritus (10022093)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Injection site rash (10022094)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Injection site warmth (10022112)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Local swelling (10024770)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Malaise (10025482)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pain (10033371)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pyrexia (10037660)	24	4.8	3.1	7.1	30	4.2	2.9	6.0	34	6.8	4.7	9.3	22	3.1	1.9	4.6
	Thirst (10043458)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Vaccination site pain (10068879)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Vaccination site rash (10069482)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Vaccination site reaction (10059080)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Vaccination site swelling (10069620)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Vessel puncture site haemorrhage (10054092)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Immune system disorders (10021428)	Drug hypersensitivity (10013700)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Hypersensitivity (10020751)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Multiple allergies (10028164)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Seasonal allergy (10048908)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Acarodermatitis (10063409)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Acute sinusitis (10001076)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	4	0.8	0.2	2.0	1	0.1	0.0	0.8
	Bronchiolitis (10006448)	8	1.6	0.7	3.1	1	0.1	0.0	0.8	13	2.6	1.4	4.4	3	0.4	0.1	1.2
	Bronchitis (10006451)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	5	1.0	0.3	2.3	4	0.6	0.2	1.4
	Candida infection (10074170)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	3	0.6	0.1	1.7	0	0.0	0.0	0.5
	Candida nappy rash (10007135)	4	0.8	0.2	2.0	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Cellulitis (10007882)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	3	0.6	0.1	1.7	0	0.0	0.0	0.5
	Clostridium difficile infection (10054236)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Conjunctivitis (10010741)	7	1.4	0.6	2.9	6	0.8	0.3	1.8	13	2.6	1.4	4.4	7	1.0	0.4	2.0
	Conjunctivitis bacterial (10061784)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Coxsackie viral infection (10011261)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Croup infectious (10011416)	8	1.6	0.7	3.1	7	1.0	0.4	2.0	8	1.6	0.7	3.1	6	0.8	0.3	1.8
	Dermatophytosis (10012504)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Ear infection (10014011)	7	1.4	0.6	2.9	3	0.4	0.1	1.2	7	1.4	0.6	2.9	4	0.6	0.2	1.4
	Enterobiasis (10014881)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Exanthema subitum (10015586)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Eye infection (10015929)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Folliculitis (10016936)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Fungal infection (10017533)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Fungal skin infection (10017543)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Gastroenteritis (10017888)	5	1.0	0.3	2.3	9	1.3	0.6	2.4	12	2.4	1.2	4.1	10	1.4	0.7	2.6
	Gastroenteritis viral (10017918)	2	0.4	0.0	1.4	2	0.3	0.0	1.0	2	0.4	0.0	1.4	2	0.3	0.0	1.0
	Genital candidiasis (10018143)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Groin abscess (10050269)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hand-foot-and-mouth disease (10019113)	1	0.2	0.0	1.1	6	0.8	0.3	1.8	2	0.4	0.0	1.4	4	0.6	0.2	1.4
	Herpangina (10019936)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Impetigo (10021531)	3	0.6	0.1	1.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Influenza (10022000)	6	1.2	0.4	2.6	1	0.1	0.0	0.8	4	0.8	0.2	2.0	3	0.4	0.1	1.2
	Lice infestation (10024424)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Localised infection (10024774)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Lower respiratory tract infection (10024968)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Molluscum contagiosum (10027807)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Nasopharyngitis (10028810)	29	5.8	3.9	8.2	37	5.2	3.7	7.1	19	3.8	2.3	5.8	35	4.9	3.4	6.7
	Neonatal candida infection (10028924)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Oral candidiasis (10030963)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Otitis externa (10033072)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Otitis media (10033078)	36	7.2	5.1	9.8	25	3.5	2.3	5.2	31	6.2	4.2	8.7	18	2.5	1.5	3.9
	Otitis media acute (10033079)	14	2.8	1.5	4.7	4	0.6	0.2	1.4	13	2.6	1.4	4.4	5	0.7	0.2	1.6
	Paronychia (10034016)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Periorbital cellulitis (10057182)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pharyngitis (10034835)	3	0.6	0.1	1.7	11	1.6	0.8	2.8	7	1.4	0.6	2.9	8	1.1	0.5	2.2
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Pharyngotonsillitis (10049140)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	2	0.4	0.0	1.4	3	0.4	0.1	1.2
	Pneumonia (10035664)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	3	0.6	0.1	1.7	3	0.4	0.1	1.2

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pneumonia mycoplasmal (10035724)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pneumonia viral (10035737)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Purulent discharge (10037569)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rash pustular (10037888)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Respiratory syncytial virus infection (10061603)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	3	0.6	0.1	1.7	1	0.1	0.0	0.8
	Respiratory tract infection (10062352)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Respiratory tract infection viral (10062106)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Rhinitis (10039083)	5	1.0	0.3	2.3	5	0.7	0.2	1.6	4	0.8	0.2	2.0	2	0.3	0.0	1.0
	Sinusitis (10040753)	3	0.6	0.1	1.7	3	0.4	0.1	1.2	5	1.0	0.3	2.3	6	0.8	0.3	1.8
	Skin candida (10054152)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Skin infection (10040872)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Staphylococcal infection (10058080)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Streptococcal infection (10061372)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Tinea capitis (10043866)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Tonsillitis (10044008)	2	0.4	0.0	1.4	2	0.3	0.0	1.0	0	0.0	0.0	0.7	6	0.8	0.3	1.8
	Tracheitis (10044302)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Upper respiratory tract infection (10046306)	62	12.4	9.6	15.6	49	6.9	5.2	9.1	65	12.9	10.1	16.2	37	5.2	3.7	7.1
	Urinary tract infection (10046571)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Varicella (10046980)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Viral infection (10047461)	5	1.0	0.3	2.3	4	0.6	0.2	1.4	7	1.4	0.6	2.9	8	1.1	0.5	2.2
	Viral rash (10047476)	11	2.2	1.1	3.9	0	0.0	0.0	0.5	2	0.4	0.0	1.4	3	0.4	0.1	1.2
	Viral upper respiratory tract infection (10047482)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	7	1.4	0.6	2.9	0	0.0	0.0	0.5

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		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Animal bite (10002515)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Arthropod bite (10003399)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Burns second degree (10006802)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Concussion (10010254)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Contusion (10050584)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Corneal abrasion (10010984)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Eyelid contusion (10075018)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Face injury (10050392)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Fall (10016173)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Foreign body (10070245)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hand fracture (10019114)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Head injury (10019196)	1	0.2	0.0	1.1	3	0.4	0.1	1.2	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Joint dislocation (10023204)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Laceration (10023572)	1	0.2	0.0	1.1	5	0.7	0.2	1.6	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Limb injury (10061225)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Mouth injury (10049294)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Procedural pain (10064882)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Radial head dislocation (10073749)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rib fracture (10039117)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Scratch (10039737)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Skin abrasion (10064990)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Tooth injury (10044043)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Upper limb fracture (10061394)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Wound (10052428)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Investigations (10022891)	Blood lead increased (10005642)	1	0.2	0.0	1.1	3	0.4	0.1	1.2	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Body temperature increased (10005911)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Heart rate increased (10019303)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	4	0.8	0.2	2.0	1	0.1	0.0	0.8

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Musculoskeletal and connective tissue disorders (10028395)	Blount's disease (10072255)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Myalgia (10028411)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pain in extremity (10033425)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Melanocytic naevus (10027145)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Skin papilloma (10040907)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Nervous system disorders (10029205)	Balance disorder (10049848)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dizziness (10013573)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Febrile convulsion (10016284)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Headache (10019211)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	3	0.4	0.1	1.2
	Psychomotor hyperactivity (10037211)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Somnolence (10041349)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Speech disorder developmental (10041467)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	3	0.6	0.1	1.7	3	0.4	0.1	1.2
	Irritability (10022998)	3	0.6	0.1	1.7	1	0.1	0.0	0.8	5	1.0	0.3	2.3	0	0.0	0.0	0.5
	Sleep disorder (10040984)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Renal and urinary disorders (10038359)	Urinary tract disorder (10046566)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Genital labial adhesions (10064162)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Genital rash (10018175)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	3	0.4	0.1	1.2
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Asthma (10003553)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Bronchial hyperreactivity (10066091)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	3	0.4	0.1	1.2
	Bronchospasm (10006482)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Cough (10011224)	27	5.4	3.6	7.8	43	6.1	4.4	8.1	41	8.2	5.9	10.9	36	5.0	3.6	6.9
	Dysphonia (10013952)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dyspnoea (10013968)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Epistaxis (10015090)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	1	0.1	0.0	0.8

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Nasal congestion (10028735)	16	3.2	1.8	5.1	9	1.3	0.6	2.4	11	2.2	1.1	3.9	8	1.1	0.5	2.2
	Nasal discharge discolouration (10071553)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Oropharyngeal pain (10068319)	2	0.4	0.0	1.4	5	0.7	0.2	1.6	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pulmonary congestion (10037368)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Respiratory disorder (10038683)	2	0.4	0.0	1.4	4	0.6	0.2	1.4	4	0.8	0.2	2.0	1	0.1	0.0	0.8
	Respiratory distress (10038687)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Respiratory tract congestion (10052251)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rhinitis allergic (10039085)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rhinorrhoea (10039101)	25	5.0	3.3	7.3	34	4.8	3.4	6.7	40	8.0	5.8	10.7	36	5.0	3.6	6.9
	Sinus congestion (10040742)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Sinus disorder (10062244)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Sneezing (10041232)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	6	1.2	0.4	2.6	4	0.6	0.2	1.4
	Wheezing (10047924)	3	0.6	0.1	1.7	2	0.3	0.0	1.0	5	1.0	0.3	2.3	3	0.4	0.1	1.2
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Blister (10005191)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Dermal cyst (10012426)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Dermatitis (10012431)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dermatitis acneiform (10012432)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Dermatitis atopic (10012438)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	3	0.6	0.1	1.7	2	0.3	0.0	1.0
	Dermatitis contact (10012442)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	3	0.6	0.1	1.7	1	0.1	0.0	0.8
	Dermatitis diaper (10012444)	18	3.6	2.1	5.6	6	0.8	0.3	1.8	11	2.2	1.1	3.9	2	0.3	0.0	1.0
	Dry skin (10013786)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Ecchymosis (10014080)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Eczema (10014184)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	5	1.0	0.3	2.3	1	0.1	0.0	0.8
	Erythema (10015150)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Hyperhidrosis (10020642)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Keratosis pilaris (10066295)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Night sweats (10029410)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Prurigo (10037083)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pruritus (10037087)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rash (10037844)	12	2.4	1.2	4.2	4	0.6	0.2	1.4	7	1.4	0.6	2.9	6	0.8	0.3	1.8
	Rash erythematous (10037855)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Rash generalised (10037858)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rash macular (10037867)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Rash papular (10037876)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rash pruritic (10037884)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Skin fissures (10040849)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Skin irritation (10040880)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Skin lesion (10040882)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Urticaria (10046735)	3	0.6	0.1	1.7	1	0.1	0.0	0.8	2	0.4	0.0	1.4	4	0.6	0.2	1.4

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 104 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		336	37.4	34.2	40.7	301	36.4	33.1	39.7	334	37.2	34.0	40.4	284	33.5	30.4	36.8
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Iron deficiency anaemia (10022972)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Leukocytosis (10024378)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Lymphadenopathy (10025197)	2	0.2	0.0	0.8	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Neutropenia (10029354)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Congenital, familial and genetic disorders (10010331)	Phimosis (10034878)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Tibial torsion (10064515)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	4	0.4	0.1	1.1	1	0.1	0.0	0.7
	Ear discomfort (10052137)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Ear pain (10014020)	2	0.2	0.0	0.8	4	0.5	0.1	1.2	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Middle ear effusion (10062545)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Dacryostenosis acquired (10053990)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Eye discharge (10015915)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Eye pruritus (10052140)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Eyelid oedema (10015993)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Lacrimation increased (10023644)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Photophobia (10034960)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Gastrointestinal disorders (10017947)	Abdominal discomfort (10000059)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Abdominal hernia (10060954)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Abdominal pain upper (10000087)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Constipation (10010774)	4	0.4	0.1	1.1	1	0.1	0.0	0.7	5	0.6	0.2	1.3	0	0.0	0.0	0.4
	Dental caries (10012318)	0	0.0	0.0	0.4	3	0.4	0.1	1.1	0	0.0	0.0	0.4	0	0.0	0.0	0.4

		Q-QIV								F-QIV							
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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Diarrhoea (10012735)	31	3.5	2.4	4.9	41	5.0	3.6	6.7	23	2.6	1.6	3.8	30	3.5	2.4	5.0
	Faeces hard (10016101)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Flatulence (10016766)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.7
	Food poisoning (10016952)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Frequent bowel movements (10017367)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Haematochezia (10018836)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Intussusception (10022863)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Nausea (10028813)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Regurgitation (10067171)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Stomatitis (10042128)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Teething (10043183)	16	1.8	1.0	2.9	2	0.2	0.0	0.9	20	2.2	1.4	3.4	2	0.2	0.0	0.9
	Vomiting (10047700)	26	2.9	1.9	4.2	22	2.7	1.7	4.0	21	2.3	1.5	3.5	26	3.1	2.0	4.5
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Administration site rash (10071156)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Asthenia (10003549)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Chills (10008531)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Developmental delay (10012559)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Discomfort (10013082)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Fatigue (10016256)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Feeling hot (10016334)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Ill-defined disorder (10061520)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Influenza like illness (10022004)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Injection site bruising (10022052)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Injection site pruritus (10022093)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Injection site rash (10022094)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Injection site warmth (10022112)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Local swelling (10024770)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Malaise (10025482)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Pain (10033371)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Pyrexia (10037660)	24	2.7	1.7	4.0	30	3.6	2.5	5.1	36	4.0	2.8	5.5	22	2.6	1.6	3.9
	Thirst (10043458)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Vaccination site pain (10068879)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Vaccination site rash (10069482)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Vaccination site reaction (10059080)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Vaccination site swelling (10069620)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Vessel puncture site haemorrhage (10054092)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Immune system disorders (10021428)	Drug hypersensitivity (10013700)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Hypersensitivity (10020751)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Multiple allergies (10028164)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Seasonal allergy (10048908)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Acarodermatitis (10063409)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Acute sinusitis (10001076)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	4	0.4	0.1	1.1	1	0.1	0.0	0.7
	Bronchiolitis (10006448)	8	0.9	0.4	1.7	1	0.1	0.0	0.7	13	1.4	0.8	2.5	3	0.4	0.1	1.0
	Bronchitis (10006451)	2	0.2	0.0	0.8	1	0.1	0.0	0.7	5	0.6	0.2	1.3	4	0.5	0.1	1.2
	Candida infection (10074170)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	3	0.3	0.1	1.0	0	0.0	0.0	0.4
	Candida nappy rash (10007135)	4	0.4	0.1	1.1	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Cellulitis (10007882)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	3	0.3	0.1	1.0	0	0.0	0.0	0.4
	Clostridium difficile infection (10054236)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Conjunctivitis (10010741)	7	0.8	0.3	1.6	6	0.7	0.3	1.6	13	1.4	0.8	2.5	7	0.8	0.3	1.7
	Conjunctivitis bacterial (10061784)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Coxsackie viral infection (10011261)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Croup infectious (10011416)	8	0.9	0.4	1.7	7	0.8	0.3	1.7	8	0.9	0.4	1.7	6	0.7	0.3	1.5
	Dermatophytosis (10012504)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Ear infection (10014011)	7	0.8	0.3	1.6	3	0.4	0.1	1.1	7	0.8	0.3	1.6	4	0.5	0.1	1.2
	Enterobiasis (10014881)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Exanthema subitum (10015586)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4

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Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Eye infection (10015929)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Folliculitis (10016936)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Fungal infection (10017533)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Fungal skin infection (10017543)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Gastroenteritis (10017888)	6	0.7	0.2	1.4	9	1.1	0.5	2.1	12	1.3	0.7	2.3	10	1.2	0.6	2.2
	Gastroenteritis viral (10017918)	2	0.2	0.0	0.8	2	0.2	0.0	0.9	2	0.2	0.0	0.8	2	0.2	0.0	0.9
	Genital candidiasis (10018143)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Groin abscess (10050269)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Hand-foot-and-mouth disease (10019113)	1	0.1	0.0	0.6	6	0.7	0.3	1.6	2	0.2	0.0	0.8	4	0.5	0.1	1.2
	Herpangina (10019936)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.7
	Impetigo (10021531)	3	0.3	0.1	1.0	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Influenza (10022000)	6	0.7	0.2	1.4	1	0.1	0.0	0.7	4	0.4	0.1	1.1	3	0.4	0.1	1.0
	Lice infestation (10024424)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Localised infection (10024774)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Lower respiratory tract infection (10024968)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Molluscum contagiosum (10027807)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Nasopharyngitis (10028810)	30	3.3	2.3	4.7	38	4.6	3.3	6.2	22	2.4	1.5	3.7	39	4.6	3.3	6.2
	Neonatal candida infection (10028924)	2	0.2	0.0	0.8	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Oral candidiasis (10030963)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Otitis externa (10033072)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Otitis media (10033078)	37	4.1	2.9	5.6	25	3.0	2.0	4.4	33	3.7	2.5	5.1	18	2.1	1.3	3.3
	Otitis media acute (10033079)	14	1.6	0.9	2.6	4	0.5	0.1	1.2	13	1.4	0.8	2.5	5	0.6	0.2	1.4
	Paronychia (10034016)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Periorbital cellulitis (10057182)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Pharyngitis (10034835)	3	0.3	0.1	1.0	11	1.3	0.7	2.4	7	0.8	0.3	1.6	8	0.9	0.4	1.9
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	1	0.1	0.0	0.6	3	0.4	0.1	1.0
	Pharyngotonsillitis (10049140)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	2	0.2	0.0	0.8	3	0.4	0.1	1.0
	Pneumonia (10035664)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	3	0.3	0.1	1.0	3	0.4	0.1	1.0
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Pneumonia mycoplasmal (10035724)	1	0.1	0.0	0.6	2	0.2	0.0	0.9	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Pneumonia viral (10035737)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Purulent discharge (10037569)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rash pustular (10037888)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Respiratory syncytial virus infection (10061603)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	3	0.3	0.1	1.0	1	0.1	0.0	0.7
	Respiratory tract infection (10062352)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Respiratory tract infection viral (10062106)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Rhinitis (10039083)	5	0.6	0.2	1.3	5	0.6	0.2	1.4	4	0.4	0.1	1.1	2	0.2	0.0	0.9
	Sinusitis (10040753)	3	0.3	0.1	1.0	3	0.4	0.1	1.1	6	0.7	0.2	1.4	6	0.7	0.3	1.5
	Skin candida (10054152)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Skin infection (10040872)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Staphylococcal infection (10058080)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Streptococcal infection (10061372)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Tinea capitis (10043866)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Tonsillitis (10044008)	2	0.2	0.0	0.8	2	0.2	0.0	0.9	0	0.0	0.0	0.4	6	0.7	0.3	1.5
	Tracheitis (10044302)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Upper respiratory tract infection (10046306)	63	7.0	5.4	8.9	51	6.2	4.6	8.0	71	7.9	6.2	9.9	37	4.4	3.1	6.0
	Urinary tract infection (10046571)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Varicella (10046980)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Viral infection (10047461)	5	0.6	0.2	1.3	4	0.5	0.1	1.2	7	0.8	0.3	1.6	8	0.9	0.4	1.9
	Viral rash (10047476)	11	1.2	0.6	2.2	0	0.0	0.0	0.4	2	0.2	0.0	0.8	3	0.4	0.1	1.0
	Viral upper respiratory tract infection (10047482)	2	0.2	0.0	0.8	1	0.1	0.0	0.7	7	0.8	0.3	1.6	0	0.0	0.0	0.4

		Q-QIV								F-QIV							
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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Animal bite (10002515)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Arthropod bite (10003399)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Burns second degree (10006802)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Concussion (10010254)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Contusion (10050584)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Corneal abrasion (10010984)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Eyelid contusion (10075018)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Face injury (10050392)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Fall (10016173)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Foreign body (10070245)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Hand fracture (10019114)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Head injury (10019196)	1	0.1	0.0	0.6	3	0.4	0.1	1.1	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Joint dislocation (10023204)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Laceration (10023572)	1	0.1	0.0	0.6	5	0.6	0.2	1.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Limb injury (10061225)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Mouth injury (10049294)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Procedural pain (10064882)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Radial head dislocation (10073749)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rib fracture (10039117)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Scratch (10039737)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Skin abrasion (10064990)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Tooth injury (10044043)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Upper limb fracture (10061394)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Wound (10052428)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Investigations (10022891)	Blood lead increased (10005642)	1	0.1	0.0	0.6	3	0.4	0.1	1.1	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Body temperature increased (10005911)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Heart rate increased (10019303)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	4	0.4	0.1	1.1	1	0.1	0.0	0.7

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Musculoskeletal and connective tissue disorders (10028395)	Blount's disease (10072255)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Myalgia (10028411)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Pain in extremity (10033425)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Melanocytic naevus (10027145)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Skin papilloma (10040907)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Nervous system disorders (10029205)	Balance disorder (10049848)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Dizziness (10013573)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Febrile convulsion (10016284)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Headache (10019211)	1	0.1	0.0	0.6	2	0.2	0.0	0.9	0	0.0	0.0	0.4	3	0.4	0.1	1.0
	Psychomotor hyperactivity (10037211)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Somnolence (10041349)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Speech disorder developmental (10041467)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	3	0.3	0.1	1.0	3	0.4	0.1	1.0
	Irritability (10022998)	3	0.3	0.1	1.0	1	0.1	0.0	0.7	5	0.6	0.2	1.3	0	0.0	0.0	0.4
	Sleep disorder (10040984)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Renal and urinary disorders (10038359)	Urinary tract disorder (10046566)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Genital labial adhesions (10064162)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Genital rash (10018175)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	3	0.4	0.1	1.0
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Asthma (10003553)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Bronchial hyperreactivity (10066091)	1	0.1	0.0	0.6	2	0.2	0.0	0.9	0	0.0	0.0	0.4	3	0.4	0.1	1.0
	Bronchospasm (10006482)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Cough (10011224)	28	3.1	2.1	4.5	44	5.3	3.9	7.1	42	4.7	3.4	6.3	36	4.3	3.0	5.8
	Dysphonia (10013952)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Dyspnoea (10013968)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Epistaxis (10015090)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	1	0.1	0.0	0.7

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Nasal congestion (10028735)	16	1.8	1.0	2.9	9	1.1	0.5	2.1	11	1.2	0.6	2.2	8	0.9	0.4	1.9
	Nasal discharge discolouration (10071553)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Oropharyngeal pain (10068319)	2	0.2	0.0	0.8	5	0.6	0.2	1.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Pulmonary congestion (10037368)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Respiratory disorder (10038683)	2	0.2	0.0	0.8	4	0.5	0.1	1.2	4	0.4	0.1	1.1	1	0.1	0.0	0.7
	Respiratory distress (10038687)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Respiratory tract congestion (10052251)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rhinitis allergic (10039085)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rhinorrhoea (10039101)	25	2.8	1.8	4.1	35	4.2	3.0	5.8	42	4.7	3.4	6.3	36	4.3	3.0	5.8
	Sinus congestion (10040742)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Sinus disorder (10062244)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Sneezing (10041232)	2	0.2	0.0	0.8	1	0.1	0.0	0.7	6	0.7	0.2	1.4	4	0.5	0.1	1.2
	Wheezing (10047924)	3	0.3	0.1	1.0	2	0.2	0.0	0.9	5	0.6	0.2	1.3	3	0.4	0.1	1.0
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Blister (10005191)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Dermal cyst (10012426)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Dermatitis (10012431)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Dermatitis acneiform (10012432)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Dermatitis atopic (10012438)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	3	0.3	0.1	1.0	2	0.2	0.0	0.9
	Dermatitis contact (10012442)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	3	0.3	0.1	1.0	1	0.1	0.0	0.7
	Dermatitis diaper (10012444)	20	2.2	1.4	3.4	6	0.7	0.3	1.6	11	1.2	0.6	2.2	2	0.2	0.0	0.9
	Dry skin (10013786)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Ecchymosis (10014080)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Eczema (10014184)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	5	0.6	0.2	1.3	1	0.1	0.0	0.7
	Erythema (10015150)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	1	0.1	0.0	0.6	3	0.4	0.1	1.0
	Hyperhidrosis (10020642)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Keratosis pilaris (10066295)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Night sweats (10029410)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Prurigo (10037083)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Pruritus (10037087)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rash (10037844)	12	1.3	0.7	2.3	4	0.5	0.1	1.2	7	0.8	0.3	1.6	7	0.8	0.3	1.7
	Rash erythematous (10037855)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Rash generalised (10037858)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rash macular (10037867)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Rash papular (10037876)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rash pruritic (10037884)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Skin fissures (10040849)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Skin irritation (10040880)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Skin lesion (10040882)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Urticaria (10046735)	3	0.3	0.1	1.0	1	0.1	0.0	0.7	2	0.2	0.0	0.8	4	0.5	0.1	1.2

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom

Table 105 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		32	6.4	4.4	8.9	38	5.4	3.8	7.3	48	9.6	7.1	12.5	27	3.8	2.5	5.4
Ear and labyrinth disorders (10013993)	Middle ear effusion (10062545)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Eye discharge (10015915)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Diarrhoea (10012735)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	2	0.4	0.0	1.4	4	0.6	0.2	1.4
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Nausea (10028813)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Stomatitis (10042128)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Vomiting (10047700)	4	0.8	0.2	2.0	5	0.7	0.2	1.6	7	1.4	0.6	2.9	6	0.8	0.3	1.8
General disorders and administration site conditions (10018065)	Chills (10008531)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Injection site pruritus (10022093)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pain (10033371)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pyrexia (10037660)	5	1.0	0.3	2.3	7	1.0	0.4	2.0	11	2.2	1.1	3.9	2	0.3	0.0	1.0
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Bronchiolitis (10006448)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	5	1.0	0.3	2.3	0	0.0	0.0	0.5
	Candida infection (10074170)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Cellulitis (10007882)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Conjunctivitis (10010741)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Croup infectious (10011416)	3	0.6	0.1	1.7	2	0.3	0.0	1.0	2	0.4	0.0	1.4	2	0.3	0.0	1.0
	Ear infection (10014011)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Gastroenteritis (10017888)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Gastroenteritis viral (10017918)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Groin abscess (10050269)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hand-foot-and-mouth disease (10019113)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Herpangina (10019936)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Influenza (10022000)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	1	0.2	0.0	1.1	1	0.1	0.0	0.8

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Nasopharyngitis (10028810)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	2	0.4	0.0	1.4	3	0.4	0.1	1.2
	Otitis media (10033078)	6	1.2	0.4	2.6	4	0.6	0.2	1.4	3	0.6	0.1	1.7	3	0.4	0.1	1.2
	Otitis media acute (10033079)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Pharyngitis (10034835)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pneumonia (10035664)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Pneumonia mycoplasmal (10035724)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rhinitis (10039083)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Sinusitis (10040753)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Staphylococcal infection (10058080)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tonsillitis (10044008)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Upper respiratory tract infection (10046306)	6	1.2	0.4	2.6	4	0.6	0.2	1.4	6	1.2	0.4	2.6	1	0.1	0.0	0.8
	Viral infection (10047461)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
Injury, poisoning and procedural complications (10022117)	Face injury (10050392)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hand fracture (10019114)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Laceration (10023572)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Mouth injury (10049294)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Radial head dislocation (10073749)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Investigations (10022891)	Heart rate increased (10019303)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Headache (10019211)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Cough (10011224)	2	0.4	0.0	1.4	2	0.3	0.0	1.0	3	0.6	0.1	1.7	3	0.4	0.1	1.2
	Dyspnoea (10013968)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Nasal congestion (10028735)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Oropharyngeal pain (10068319)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Respiratory disorder (10038683)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Rhinorrhoea (10039101)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Wheezing (10047924)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dermatitis diaper (10012444)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Rash (10037844)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Urticaria (10046735)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 106 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		34	3.8	2.6	5.3	38	4.6	3.3	6.2	52	5.8	4.3	7.5	27	3.2	2.1	4.6
Ear and labyrinth disorders (10013993)	Middle ear effusion (10062545)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Eye discharge (10015915)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Diarrhoea (10012735)	0	0.0	0.0	0.4	3	0.4	0.1	1.1	2	0.2	0.0	0.8	4	0.5	0.1	1.2
	Intussusception (10022863)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Nausea (10028813)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Stomatitis (10042128)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Vomiting (10047700)	4	0.4	0.1	1.1	5	0.6	0.2	1.4	7	0.8	0.3	1.6	6	0.7	0.3	1.5
General disorders and administration site conditions (10018065)	Chills (10008531)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Injection site pruritus (10022093)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Pain (10033371)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Pyrexia (10037660)	5	0.6	0.2	1.3	7	0.8	0.3	1.7	12	1.3	0.7	2.3	2	0.2	0.0	0.9
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Bronchiolitis (10006448)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	5	0.6	0.2	1.3	0	0.0	0.0	0.4
	Candida infection (10074170)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Cellulitis (10007882)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Conjunctivitis (10010741)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Croup infectious (10011416)	3	0.3	0.1	1.0	2	0.2	0.0	0.9	2	0.2	0.0	0.8	2	0.2	0.0	0.9
	Ear infection (10014011)	2	0.2	0.0	0.8	1	0.1	0.0	0.7	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Gastroenteritis (10017888)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Gastroenteritis viral (10017918)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Groin abscess (10050269)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Hand-foot-and-mouth disease (10019113)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Herpangina (10019936)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Influenza (10022000)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Nasopharyngitis (10028810)	1	0.1	0.0	0.6	2	0.2	0.0	0.9	2	0.2	0.0	0.8	3	0.4	0.1	1.0

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Otitis media (10033078)	6	0.7	0.2	1.4	4	0.5	0.1	1.2	3	0.3	0.1	1.0	3	0.4	0.1	1.0
	Otitis media acute (10033079)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Pharyngitis (10034835)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Pneumonia (10035664)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Pneumonia mycoplasmal (10035724)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rhinitis (10039083)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Sinusitis (10040753)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Staphylococcal infection (10058080)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Tonsillitis (10044008)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Upper respiratory tract infection (10046306)	6	0.7	0.2	1.4	4	0.5	0.1	1.2	6	0.7	0.2	1.4	1	0.1	0.0	0.7
	Viral infection (10047461)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	2	0.2	0.0	0.8	1	0.1	0.0	0.7
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
Injury, poisoning and procedural complications (10022117)	Face injury (10050392)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Hand fracture (10019114)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Laceration (10023572)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Mouth injury (10049294)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Radial head dislocation (10073749)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Investigations (10022891)	Heart rate increased (10019303)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Headache (10019211)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Somnolence (10041349)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.7
	Irritability (10022998)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Cough (10011224)	2	0.2	0.0	0.8	2	0.2	0.0	0.9	3	0.3	0.1	1.0	3	0.4	0.1	1.0
	Dyspnoea (10013968)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Nasal congestion (10028735)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Oropharyngeal pain (10068319)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Respiratory disorder (10038683)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Rhinorrhoea (10039101)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	3	0.4	0.1	1.0
	Wheezing (10047924)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Dermatitis diaper (10012444)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Rash (10037844)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Urticaria (10046735)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.7

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 107 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		36	7.2	5.1	9.8	35	5.0	3.5	6.8	33	6.6	4.6	9.1	38	5.3	3.8	7.2
Blood and lymphatic system disorders (10005329)	Lymphadenopathy (10025197)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Ear and labyrinth disorders (10013993)	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Eye disorders (10015919)	Eye discharge (10015915)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Lacrimation increased (10023644)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Diarrhoea (10012735)	5	1.0	0.3	2.3	7	1.0	0.4	2.0	5	1.0	0.3	2.3	8	1.1	0.5	2.2
	Vomiting (10047700)	9	1.8	0.8	3.4	4	0.6	0.2	1.4	4	0.8	0.2	2.0	9	1.3	0.6	2.4
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Administration site rash (10071156)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Chills (10008531)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Feeling hot (10016334)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Injection site bruising (10022052)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Injection site rash (10022094)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Injection site warmth (10022112)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Local swelling (10024770)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Malaise (10025482)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pain (10033371)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pyrexia (10037660)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	4	0.8	0.2	2.0	0	0.0	0.0	0.5
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Immune system disorders (10021428)	Multiple allergies (10028164)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Infections and infestations (10021881)	Conjunctivitis (10010741)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Croup infectious (10011416)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Influenza (10022000)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Nasopharyngitis (10028810)	2	0.4	0.0	1.4	3	0.4	0.1	1.2	1	0.2	0.0	1.1	2	0.3	0.0	1.0
	Otitis media (10033078)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Pharyngitis (10034835)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rhinitis (10039083)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Upper respiratory tract infection (10046306)	5	1.0	0.3	2.3	4	0.6	0.2	1.4	4	0.8	0.2	2.0	0	0.0	0.0	0.5
	Viral infection (10047461)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Nervous system disorders (10029205)	Headache (10019211)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	2	0.4	0.0	1.4	4	0.6	0.2	1.4	6	1.2	0.4	2.6	6	0.8	0.3	1.8
	Nasal congestion (10028735)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	4	0.8	0.2	2.0	3	0.4	0.1	1.2
	Rhinorrhoea (10039101)	6	1.2	0.4	2.6	3	0.4	0.1	1.2	9	1.8	0.8	3.4	6	0.8	0.3	1.8
	Sneezing (10041232)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Wheezing (10047924)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Skin and subcutaneous tissue disorders (10040785)	Dermatitis acneiform (10012432)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Dermatitis diaper (10012444)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Erythema (10015150)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Hyperhidrosis (10020642)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Rash (10037844)	3	0.6	0.1	1.7	3	0.4	0.1	1.2	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rash generalised (10037858)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rash papular (10037876)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Skin fissures (10040849)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Urticaria (10046735)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	3	0.4	0.1	1.2

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 108 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		39	4.3	3.1	5.9	36	4.3	3.1	6.0	35	3.9	2.7	5.4	38	4.5	3.2	6.1
Blood and lymphatic system disorders (10005329)	Lymphadenopathy (10025197)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Ear and labyrinth disorders (10013993)	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Lacrimation increased (10023644)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Diarrhoea (10012735)	6	0.7	0.2	1.4	7	0.8	0.3	1.7	5	0.6	0.2	1.3	8	0.9	0.4	1.9
	Vomiting (10047700)	9	1.0	0.5	1.9	4	0.5	0.1	1.2	4	0.4	0.1	1.1	9	1.1	0.5	2.0
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
	Administration site rash (10071156)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Chills (10008531)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Feeling hot (10016334)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Injection site bruising (10022052)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Injection site rash (10022094)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Injection site warmth (10022112)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Local swelling (10024770)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Malaise (10025482)	0	0.0	0.0	0.4	2	0.2	0.0	0.9	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Pain (10033371)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Pyrexia (10037660)	2	0.2	0.0	0.8	0	0.0	0.0	0.4	4	0.4	0.1	1.1	0	0.0	0.0	0.4
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Immune system disorders (10021428)	Multiple allergies (10028164)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Infections and infestations (10021881)	Conjunctivitis (10010741)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Croup infectious (10011416)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Influenza (10022000)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Nasopharyngitis (10028810)	2	0.2	0.0	0.8	3	0.4	0.1	1.1	1	0.1	0.0	0.6	2	0.2	0.0	0.9
	Otitis media (10033078)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Pharyngitis (10034835)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	1	0.1	0.0	0.6	0	0.0	0.0	0.4

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rhinitis (10039083)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Upper respiratory tract infection (10046306)	5	0.6	0.2	1.3	4	0.5	0.1	1.2	4	0.4	0.1	1.1	0	0.0	0.0	0.4
	Viral infection (10047461)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Nervous system disorders (10029205)	Headache (10019211)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Somnolence (10041349)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	1	0.1	0.0	0.7
	Irritability (10022998)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.8	0	0.0	0.0	0.4
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	2	0.2	0.0	0.8	4	0.5	0.1	1.2	6	0.7	0.2	1.4	6	0.7	0.3	1.5
	Nasal congestion (10028735)	1	0.1	0.0	0.6	2	0.2	0.0	0.9	4	0.4	0.1	1.1	3	0.4	0.1	1.0
	Rhinorrhoea (10039101)	6	0.7	0.2	1.4	3	0.4	0.1	1.1	10	1.1	0.5	2.0	6	0.7	0.3	1.5
	Sneezing (10041232)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	2	0.2	0.0	0.8	1	0.1	0.0	0.7
	Wheezing (10047924)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
Skin and subcutaneous tissue disorders (10040785)	Dermatitis acneiform (10012432)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Dermatitis diaper (10012444)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Erythema (10015150)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	2	0.2	0.0	0.9
	Hyperhidrosis (10020642)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Rash (10037844)	3	0.3	0.1	1.0	3	0.4	0.1	1.1	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rash generalised (10037858)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Rash papular (10037876)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Skin fissures (10040849)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Urticaria (10046735)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	3	0.4	0.1	1.0

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom

Table 109 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		5	1.0	0.3	2.3	2	0.3	0.0	1.0	4	0.8	0.2	2.0	5	0.7	0.2	1.6
Eye disorders (10015919)	Eye discharge (10015915)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Vomiting (10047700)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	1	0.2	0.0	1.1	2	0.3	0.0	1.0
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Nasopharyngitis (10028810)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Otitis media (10033078)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Upper respiratory tract infection (10046306)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Viral infection (10047461)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Nervous system disorders (10029205)	Somnolence (10041349)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Rhinorrhoea (10039101)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Wheezing (10047924)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 110 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 898				18-35M N = 828				6-17M N = 899				18-35M N = 847			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		5	0.6	0.2	1.3	2	0.2	0.0	0.9	4	0.4	0.1	1.1	5	0.6	0.2	1.4
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	0	0.0	0.0	0.4	1	0.1	0.0	0.7	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Vomiting (10047700)	1	0.1	0.0	0.6	1	0.1	0.0	0.7	1	0.1	0.0	0.6	2	0.2	0.0	0.9
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Nasopharyngitis (10028810)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Otitis media (10033078)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Upper respiratory tract infection (10046306)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4
	Viral infection (10047461)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Nervous system disorders (10029205)	Somnolence (10041349)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Irritability (10022998)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.6	0	0.0	0.0	0.4
	Rhinorrhoea (10039101)	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4	1	0.1	0.0	0.7
	Wheezing (10047924)	1	0.1	0.0	0.6	0	0.0	0.0	0.4	0	0.0	0.0	0.4	0	0.0	0.0	0.4

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 111 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit (MAEs) during the entire study period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		322	64.4	60.0	68.6	405	57.3	53.5	61.0	323	64.3	60.0	68.5	396	55.4	51.7	59.1
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	5	1.0	0.3	2.3	2	0.3	0.0	1.0
	Iron deficiency anaemia (10022972)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	2	0.3	0.0	1.0
	Leukocytosis (10024378)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	3	0.4	0.1	1.2
	Lymphadenitis (10025188)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Lymphadenopathy (10025197)	2	0.4	0.0	1.4	4	0.6	0.2	1.4	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Neutropenia (10029354)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Congenital, familial and genetic disorders (10010331)	Cryptorchism (10011498)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Cytogenetic abnormality (10067477)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dermoid cyst (10012522)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Macrocephaly (10050183)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Phimosis (10034878)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Tibial torsion (10064515)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	4	0.8	0.2	2.0	6	0.8	0.3	1.8	6	1.2	0.4	2.6	5	0.7	0.2	1.6
	Deafness bilateral (10052556)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Deafness unilateral (10048812)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Ear discomfort (10052137)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Ear disorder (10014004)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Ear pain (10014020)	4	0.8	0.2	2.0	9	1.3	0.6	2.4	5	1.0	0.3	2.3	9	1.3	0.6	2.4

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Eustachian tube dysfunction (10015543)	3	0.6	0.1	1.7	3	0.4	0.1	1.2	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Eustachian tube obstruction (10015544)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Middle ear effusion (10062545)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Otorrhoea (10033101)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Tympanic membrane hyperaemia (10052154)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
Eye disorders (10015919)	Astigmatism (10003569)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Blepharitis (10005148)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Chalazion (10008388)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Conjunctival haemorrhage (10010719)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Conjunctivitis allergic (10010744)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Dacryostenosis acquired (10053990)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Eye discharge (10015915)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Eyelid oedema (10015993)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Photophobia (10034960)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Strabismus (10042159)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Gastrointestinal disorders (10017947)	Abdominal hernia (10060954)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Abdominal pain (10000081)	0	0.0	0.0	0.7	4	0.6	0.2	1.4	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Abdominal pain upper (10000087)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Anal fissure (10002153)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Anal polyp (10002168)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Anal pruritus (10068172)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Anal skin tags (10002172)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Constipation (10010774)	4	0.8	0.2	2.0	3	0.4	0.1	1.2	7	1.4	0.6	2.9	3	0.4	0.1	1.2
	Dental caries (10012318)	0	0.0	0.0	0.7	4	0.6	0.2	1.4	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Diarrhoea (10012735)	24	4.8	3.1	7.1	15	2.1	1.2	3.5	25	5.0	3.2	7.3	15	2.1	1.2	3.4
	Epigastric discomfort (10053155)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Eructation (10015137)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Flatulence (10016766)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Food poisoning (10016952)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Gastrointestinal inflammation (10064147)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Gastrooesophageal reflux disease (10017885)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Haematochezia (10018836)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Nausea (10028813)	4	0.8	0.2	2.0	2	0.3	0.0	1.0	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Oral disorder (10067621)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Post-tussive vomiting (10066220)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Stomatitis (10042128)	1	0.2	0.0	1.1	4	0.6	0.2	1.4	2	0.4	0.0	1.4	2	0.3	0.0	1.0
	Teething (10043183)	7	1.4	0.6	2.9	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Vomiting (10047700)	26	5.2	3.4	7.5	18	2.5	1.5	4.0	19	3.8	2.3	5.8	17	2.4	1.4	3.8
General disorders and administration site conditions (10018065)	Asthenia (10003549)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	1	0.2	0.0	1.1	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Crying (10011469)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Developmental delay (10012559)	1	0.2	0.0	1.1	3	0.4	0.1	1.2	3	0.6	0.1	1.7	2	0.3	0.0	1.0
	Fatigue (10016256)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Gait disturbance (10017577)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Influenza like illness (10022004)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	1	0.2	0.0	1.1	2	0.3	0.0	1.0
	Local swelling (10024770)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pyrexia (10037660)	35	7.0	4.9	9.6	40	5.7	4.1	7.6	43	8.6	6.3	11.4	29	4.1	2.7	5.8
	Vaccination site rash (10069482)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Vaccination site reaction (10059080)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Vessel puncture site haemorrhage (10054092)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Immune system disorders (10021428)	Allergy to animal (10001742)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Drug hypersensitivity (10013700)	4	0.8	0.2	2.0	1	0.1	0.0	0.8	1	0.2	0.0	1.1	4	0.6	0.2	1.4
	Food allergy (10016946)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hypersensitivity (10020751)	2	0.4	0.0	1.4	2	0.3	0.0	1.0	3	0.6	0.1	1.7	1	0.1	0.0	0.8
	Immunodeficiency (10061598)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Multiple allergies (10028164)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Seasonal allergy (10048908)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Selective iga immunodeficiency (10039915)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Infections and infestations (10021881)	Abscess (10000269)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Abscess limb (10050473)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Acarodermatitis (10063409)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	3	0.4	0.1	1.2
	Acute sinusitis (10001076)	3	0.6	0.1	1.7	7	1.0	0.4	2.0	7	1.4	0.6	2.9	7	1.0	0.4	2.0
	Acute tonsillitis (10001093)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Adenoiditis (10051223)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5

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		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Atypical mycobacterial infection (10061663)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Body tinea (10005913)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	1	0.2	0.0	1.1	2	0.3	0.0	1.0
	Bronchiolitis (10006448)	24	4.8	3.1	7.1	13	1.8	1.0	3.1	26	5.2	3.4	7.5	10	1.4	0.7	2.6
	Bronchitis (10006451)	4	0.8	0.2	2.0	6	0.8	0.3	1.8	8	1.6	0.7	3.1	17	2.4	1.4	3.8
	Candida infection (10074170)	3	0.6	0.1	1.7	1	0.1	0.0	0.8	7	1.4	0.6	2.9	0	0.0	0.0	0.5
	Candida nappy rash (10007135)	8	1.6	0.7	3.1	2	0.3	0.0	1.0	3	0.6	0.1	1.7	2	0.3	0.0	1.0
	Cellulitis (10007882)	3	0.6	0.1	1.7	3	0.4	0.1	1.2	4	0.8	0.2	2.0	4	0.6	0.2	1.4
	Clostridium difficile infection (10054236)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Conjunctivitis (10010741)	22	4.4	2.8	6.6	34	4.8	3.4	6.7	33	6.6	4.6	9.1	32	4.5	3.1	6.3
	Conjunctivitis bacterial (10061784)	3	0.6	0.1	1.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Conjunctivitis viral (10010755)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Coxsackie viral infection (10011261)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Croup infectious (10011416)	23	4.6	2.9	6.8	35	5.0	3.5	6.8	23	4.6	2.9	6.8	24	3.4	2.2	5.0
	Dacryocystitis (10011844)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Dermatophytosis (10012504)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Ear infection (10014011)	10	2.0	1.0	3.6	6	0.8	0.3	1.8	9	1.8	0.8	3.4	8	1.1	0.5	2.2
	Enterobiasis (10014881)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Exanthema subitum (10015586)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	3	0.6	0.1	1.7	0	0.0	0.0	0.5
	External ear cellulitis (10015729)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Eye infection (10015929)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Folliculitis (10016936)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	4	0.6	0.2	1.4
	Fungal infection (10017533)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	2	0.3	0.0	1.0

		Q-QIV								F-QIV							
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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Fungal skin infection (10017543)	4	0.8	0.2	2.0	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Furuncle (10017553)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Gastroenteritis (10017888)	25	5.0	3.3	7.3	34	4.8	3.4	6.7	29	5.8	3.9	8.2	38	5.3	3.8	7.2
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Gastroenteritis viral (10017918)	8	1.6	0.7	3.1	11	1.6	0.8	2.8	5	1.0	0.3	2.3	0	0.0	0.0	0.5
	Genital candidiasis (10018143)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Groin abscess (10050269)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hand-foot-and-mouth disease (10019113)	3	0.6	0.1	1.7	7	1.0	0.4	2.0	6	1.2	0.4	2.6	7	1.0	0.4	2.0
	Herpangina (10019936)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	3	0.6	0.1	1.7	1	0.1	0.0	0.8
	Hordeolum (10020377)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Impetigo (10021531)	2	0.4	0.0	1.4	5	0.7	0.2	1.6	3	0.6	0.1	1.7	4	0.6	0.2	1.4
	Infected bites (10021769)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Influenza (10022000)	12	2.4	1.2	4.2	11	1.6	0.8	2.8	14	2.8	1.5	4.6	14	2.0	1.1	3.3
	Laryngitis (10023874)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Lice infestation (10024424)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Localised infection (10024774)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Lower respiratory tract infection (10024968)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Molluscum contagiosum (10027807)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	4	0.6	0.2	1.4
	Myringitis bullous (10028659)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Nasopharyngitis (10028810)	18	3.6	2.1	5.6	33	4.7	3.2	6.5	14	2.8	1.5	4.6	32	4.5	3.1	6.3
	Neonatal candida infection (10028924)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Onychomycosis (10030338)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Oral candidiasis (10030963)	4	0.8	0.2	2.0	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Oropharyngeal candidiasis (10050346)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Otitis externa (10033072)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Otitis media (10033078)	102	20.4	17.0	24.2	92	13.0	10.6	15.7	116	23.1	19.5	27.0	106	14.8	12.3	17.6
	Otitis media acute (10033079)	34	6.8	4.8	9.4	31	4.4	3.0	6.2	44	8.8	6.4	11.6	24	3.4	2.2	5.0
	Otitis media chronic (10033081)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	2	0.4	0.0	1.4	4	0.6	0.2	1.4
	Paronychia (10034016)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Penile infection (10061912)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Periorbital cellulitis (10057182)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Pharyngitis (10034835)	13	2.6	1.4	4.4	31	4.4	3.0	6.2	18	3.6	2.1	5.6	29	4.1	2.7	5.8
	Pharyngitis streptococcal (10034839)	6	1.2	0.4	2.6	15	2.1	1.2	3.5	5	1.0	0.3	2.3	18	2.5	1.5	3.9
	Pharyngotonsillitis (10049140)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	3	0.6	0.1	1.7	3	0.4	0.1	1.2
	Pneumonia (10035664)	8	1.6	0.7	3.1	14	2.0	1.1	3.3	9	1.8	0.8	3.4	17	2.4	1.4	3.8
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Pneumonia mycoplasmal (10035724)	1	0.2	0.0	1.1	3	0.4	0.1	1.2	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Pneumonia viral (10035737)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pseudomonas infection (10061471)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Rash pustular (10037888)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Respiratory syncytial virus bronchiolitis (10038718)	5	1.0	0.3	2.3	1	0.1	0.0	0.8	3	0.6	0.1	1.7	2	0.3	0.0	1.0
	Respiratory syncytial virus infection (10061603)	7	1.4	0.6	2.9	8	1.1	0.5	2.2	8	1.6	0.7	3.1	7	1.0	0.4	2.0

		Q-QIV								F-QIV							
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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Respiratory tract infection (10062352)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	3	0.6	0.1	1.7	0	0.0	0.0	0.5
	Respiratory tract infection viral (10062106)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Rhinitis (10039083)	4	0.8	0.2	2.0	4	0.6	0.2	1.4	6	1.2	0.4	2.6	2	0.3	0.0	1.0
	Roseola (10039222)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Rotavirus infection (10067470)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Scarlet fever (10039587)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Sinusitis (10040753)	13	2.6	1.4	4.4	18	2.5	1.5	4.0	19	3.8	2.3	5.8	24	3.4	2.2	5.0
	Sinusitis bacterial (10060841)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Skin candida (10054152)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	3	0.6	0.1	1.7	1	0.1	0.0	0.8
	Skin infection (10040872)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Staphylococcal infection (10058080)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	3	0.4	0.1	1.2
	Streptococcal infection (10061372)	1	0.2	0.0	1.1	3	0.4	0.1	1.2	2	0.4	0.0	1.4	3	0.4	0.1	1.2
	Subcutaneous abscess (10042343)	3	0.6	0.1	1.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Tinea capitis (10043866)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Tinea infection (10060889)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tonsillitis (10044008)	3	0.6	0.1	1.7	7	1.0	0.4	2.0	2	0.4	0.0	1.4	9	1.3	0.6	2.4
	Tonsillitis streptococcal (10044013)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Tooth infection (10048762)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tracheitis (10044302)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tracheobronchitis viral (10061556)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Upper respiratory tract infection (10046306)	121	24.2	20.5	28.2	122	17.3	14.5	20.2	129	25.7	21.9	29.8	104	14.5	12.0	17.3

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Urinary tract infection (10046571)	4	0.8	0.2	2.0	4	0.6	0.2	1.4	5	1.0	0.3	2.3	6	0.8	0.3	1.8
	Vaginal infection (10046914)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Varicella (10046980)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Viral infection (10047461)	28	5.6	3.8	8.0	26	3.7	2.4	5.3	28	5.6	3.7	8.0	26	3.6	2.4	5.3
	Viral pharyngitis (10047473)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	2	0.4	0.0	1.4	2	0.3	0.0	1.0
	Viral rash (10047476)	17	3.4	2.0	5.4	1	0.1	0.0	0.8	12	2.4	1.2	4.1	6	0.8	0.3	1.8
	Viral tonsillitis (10047480)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Viral upper respiratory tract infection (10047482)	13	2.6	1.4	4.4	5	0.7	0.2	1.6	13	2.6	1.4	4.4	9	1.3	0.6	2.4
	Vulvovaginitis (10047794)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Wound infection (10048038)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Animal bite (10002515)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Arthropod bite (10003399)	2	0.4	0.0	1.4	5	0.7	0.2	1.6	0	0.0	0.0	0.7	4	0.6	0.2	1.4
	Burns first degree (10006797)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Burns second degree (10006802)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Clavicle fracture (10009245)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Concussion (10010254)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Contusion (10050584)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Corneal abrasion (10010984)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Craniocerebral injury (10070976)	1	0.2	0.0	1.1	3	0.4	0.1	1.2	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Exposure to communicable disease (10049711)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Exposure to toxic agent (10053487)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Face injury (10050392)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Fall (10016173)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Foreign body (10070245)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Hand fracture (10019114)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Head injury (10019196)	2	0.4	0.0	1.4	9	1.3	0.6	2.4	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Humerus fracture (10020462)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Injury (10022116)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Joint dislocation (10023204)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Joint injury (10060820)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Laceration (10023572)	4	0.8	0.2	2.0	12	1.7	0.9	2.9	0	0.0	0.0	0.7	8	1.1	0.5	2.2
	Ligament sprain (10024453)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Limb crushing injury (10064031)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Limb injury (10061225)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Lip injury (10055082)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Mouth injury (10049294)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Multiple injuries (10028224)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Procedural pain (10064882)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Radial head dislocation (10073749)	0	0.0	0.0	0.7	3	0.4	0.1	1.2	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Rib fracture (10039117)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Road traffic accident (10039203)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Skin abrasion (10064990)	1	0.2	0.0	1.1	3	0.4	0.1	1.2	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Splinter (10041662)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Thermal burn (10053615)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tooth injury (10044043)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Ulna fracture (10045375)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Upper limb fracture (10061394)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Vaccination complication (10046861)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Wound (10052428)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Wound complication (10053692)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Investigations (10022891)	Blood carbon monoxide (10005406)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Blood lead increased (10005642)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Body temperature increased (10005911)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Cardiac murmur (10007586)	0	0.0	0.0	0.7	4	0.6	0.2	1.4	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Heart rate increased (10019303)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Weight increased (10047899)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Metabolism and nutrition disorders (10027433)	Abnormal weight gain (10000188)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Breast milk substitute intolerance (10072187)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Decreased appetite (10061428)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	1	0.2	0.0	1.1	5	0.7	0.2	1.6
	Dehydration (10012174)	6	1.2	0.4	2.6	3	0.4	0.1	1.2	3	0.6	0.1	1.7	3	0.4	0.1	1.2
	Failure to thrive (10016165)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Feeding disorder (10061148)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Feeding disorder of infancy or early childhood (10016318)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Hyponatraemia (10021036)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Lactose intolerance (10023681)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Obesity (10029883)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Overweight (10033307)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Pica (10035001)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Back pain (10003988)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Blount's disease (10072255)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Flank pain (10016750)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Foot deformity (10061159)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Growing pains (10018745)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Growth retardation (10053759)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Head deformity (10061199)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Joint swelling (10023232)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Knee deformity (10062061)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Musculoskeletal pain (10028391)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pain in extremity (10033425)	2	0.4	0.0	1.4	3	0.4	0.1	1.2	2	0.4	0.0	1.4	2	0.3	0.0	1.0
	Synovial cyst (10042858)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Tenosynovitis (10043261)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Torticollis (10044074)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	B precursor type acute leukaemia (10003890)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Haemangioma (10018814)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Melanocytic naevus (10027145)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Skin papilloma (10040907)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	4	0.6	0.2	1.4

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Nervous system disorders (10029205)	Febrile convulsion (10016284)	2	0.4	0.0	1.4	3	0.4	0.1	1.2	2	0.4	0.0	1.4	2	0.3	0.0	1.0
	Fine motor delay (10066088)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Gross motor delay (10069118)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Hemiplegia (10019468)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Language disorder (10074869)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Motor developmental delay (10070302)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Presyncope (10036653)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Seizure (10039906)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Sensory integrative dysfunction (10048871)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Speech disorder (10041466)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Speech disorder developmental (10041467)	2	0.4	0.0	1.4	5	0.7	0.2	1.6	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Tremor (10044565)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Pregnancy, puerperium and perinatal conditions (10036585)	Cephalhaematoma (10008014)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Psychiatric disorders (10037175)	Abnormal behaviour (10061422)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Autism spectrum disorder (10063844)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Eating disorder (10014062)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Head banging (10019191)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Irritability (10022998)	3	0.6	0.1	1.7	3	0.4	0.1	1.2	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Libido disorder (10061221)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Middle insomnia (10027590)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Onychophagia (10057342)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Phonological disorder (10034925)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Sleep disorder (10040984)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Renal and urinary disorders (10038359)	Calculus urinary (10007027)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dysuria (10013990)	0	0.0	0.0	0.7	4	0.6	0.2	1.4	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Enuresis (10014928)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pollakiuria (10036018)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Urinary incontinence (10046543)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Urinary tract disorder (10046566)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Urine odour abnormal (10057135)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Genital erythema (10054816)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Genital labial adhesions (10064162)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	5	1.0	0.3	2.3	0	0.0	0.0	0.5
	Genital rash (10018175)	5	1.0	0.3	2.3	0	0.0	0.0	0.5	2	0.4	0.0	1.4	4	0.6	0.2	1.4
	Gynaecomastia (10018800)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Penile adhesion (10059636)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Pruritus genital (10037093)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Testicular retraction (10043348)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Vaginal discharge (10046901)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	1	0.2	0.0	1.1	2	0.3	0.0	1.0	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Asthma (10003553)	3	0.6	0.1	1.7	7	1.0	0.4	2.0	4	0.8	0.2	2.0	17	2.4	1.4	3.8
	Bronchial hyperreactivity (10066091)	7	1.4	0.6	2.9	5	0.7	0.2	1.6	2	0.4	0.0	1.4	10	1.4	0.7	2.6

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Bronchospasm (10006482)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	2	0.4	0.0	1.4	0	0.0	0.0	0.5
	Cough (10011224)	20	4.0	2.5	6.1	26	3.7	2.4	5.3	31	6.2	4.2	8.7	33	4.6	3.2	6.4
	Dyspnoea (10013968)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Epistaxis (10015090)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	3	0.4	0.1	1.2
	Hypoxia (10021143)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Lower respiratory tract congestion (10075565)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Nasal congestion (10028735)	11	2.2	1.1	3.9	3	0.4	0.1	1.2	8	1.6	0.7	3.1	7	1.0	0.4	2.0
	Nasal discomfort (10052437)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Oropharyngeal pain (10068319)	2	0.4	0.0	1.4	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pneumonitis (10035742)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pulmonary congestion (10037368)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Respiratory disorder (10038683)	2	0.4	0.0	1.4	5	0.7	0.2	1.6	8	1.6	0.7	3.1	5	0.7	0.2	1.6
	Respiratory distress (10038687)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rhinitis allergic (10039085)	8	1.6	0.7	3.1	6	0.8	0.3	1.8	4	0.8	0.2	2.0	8	1.1	0.5	2.2
	Rhinorrhoea (10039101)	5	1.0	0.3	2.3	3	0.4	0.1	1.2	9	1.8	0.8	3.4	7	1.0	0.4	2.0
	Sinus congestion (10040742)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Sinus disorder (10062244)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	2	0.3	0.0	1.0
	Sleep apnoea syndrome (10040979)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	3	0.6	0.1	1.7	0	0.0	0.0	0.5
	Sneezing (10041232)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Snoring (10041235)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Tonsillar hypertrophy (10044003)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Upper-airway cough syndrome (10070488)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Wheezing (10047924)	10	2.0	1.0	3.6	10	1.4	0.7	2.6	7	1.4	0.6	2.9	5	0.7	0.2	1.6

		Q-QIV								F-QIV							
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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Blister (10005191)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Cafe au lait spots (10006926)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Dermal cyst (10012426)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Dermatitis (10012431)	5	1.0	0.3	2.3	3	0.4	0.1	1.2	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Dermatitis atopic (10012438)	4	0.8	0.2	2.0	3	0.4	0.1	1.2	8	1.6	0.7	3.1	8	1.1	0.5	2.2
	Dermatitis contact (10012442)	2	0.4	0.0	1.4	1	0.1	0.0	0.8	4	0.8	0.2	2.0	3	0.4	0.1	1.2
	Dermatitis diaper (10012444)	20	4.0	2.5	6.1	11	1.6	0.8	2.8	18	3.6	2.1	5.6	5	0.7	0.2	1.6
	Dry skin (10013786)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Ecchymosis (10014080)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Eczema (10014184)	3	0.6	0.1	1.7	1	0.1	0.0	0.8	15	3.0	1.7	4.9	2	0.3	0.0	1.0
	Eczema nummular (10014201)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Erythema (10015150)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Erythema multiforme (10015218)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Hand dermatitis (10058898)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Idiopathic urticaria (10021247)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Ingrowing nail (10022013)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Keratosis pilaris (10066295)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Miliaria (10027627)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Nail disorder (10028694)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Neurodermatitis (10029263)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Petechiae (10034754)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Prurigo (10037083)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Rash (10037844)	9	1.8	0.8	3.4	5	0.7	0.2	1.6	4	0.8	0.2	2.0	10	1.4	0.7	2.6
	Rash erythematous (10037855)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Rash generalised (10037858)	0	0.0	0.0	0.7	2	0.3	0.0	1.0	1	0.2	0.0	1.1	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rash macular (10037867)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Skin fissures (10040849)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Skin lesion (10040882)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Solar urticaria (10041307)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Urticaria (10046735)	8	1.6	0.7	3.1	9	1.3	0.6	2.4	4	0.8	0.2	2.0	6	0.8	0.3	1.8
	Urticaria papular (10046750)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Social circumstances (10041244)	Sexual abuse (10040461)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Surgical and medical procedures (10042613)	Adenoidectomy (10001230)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Umbilical hernia repair (10045462)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Vascular disorders (10047065)	Haematoma (10018852)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Kawasaki's disease (10023320)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pallor (10033546)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 112 Percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire study period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Skin and subcutaneous tissue disorders (10040785)	Erythema multiforme (10015218)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Vascular disorders (10047065)	Kawasaki's disease (10023320)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 113 Percentage of subjects reporting the occurrence of serious adverse events (SAEs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire study period by age strata (Total vaccinated cohort)

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		11	2.2	1.1	3.9	11	1.6	0.8	2.8	11	2.2	1.1	3.9	10	1.4	0.7	2.6
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
General disorders and administration site conditions (10018065)	Developmental delay (10012559)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Bronchiolitis (10006448)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	1	0.1	0.0	0.8
	Cellulitis (10007882)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Croup infectious (10011416)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Gastroenteritis (10017888)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.0
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Groin abscess (10050269)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Lower respiratory tract infection (10024968)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Otitis media acute (10033079)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pharyngitis (10034835)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Pneumonia (10035664)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Respiratory syncytial virus bronchiolitis (10038718)	2	0.4	0.0	1.4	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Respiratory syncytial virus infection (10061603)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Urinary tract infection (10046571)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Concussion (10010254)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Craniocerebral injury (10070976)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Multiple injuries (10028224)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5

		Q-QIV								F-QIV							
		6-17M N = 500				18-35M N = 707				6-17M N = 502				18-35M N = 715			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	2	0.4	0.0	1.4	1	0.1	0.0	0.8
	Failure to thrive (10016165)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Hyponatraemia (10021036)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	B precursor type acute leukaemia (10003890)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	2	0.4	0.0	1.4	3	0.4	0.1	1.2	2	0.4	0.0	1.4	2	0.3	0.0	1.0
	Hemiplegia (10019468)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	0	0.0	0.0	0.7	1	0.1	0.0	0.8
	Seizure (10039906)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Renal and urinary disorders (10038359)	Calculus urinary (10007027)	0	0.0	0.0	0.7	0	0.0	0.0	0.5	1	0.2	0.0	1.1	0	0.0	0.0	0.5
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	1	0.2	0.0	1.1	1	0.1	0.0	0.8	1	0.2	0.0	1.1	0	0.0	0.0	0.5
	Hypoxia (10021143)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
	Pneumonitis (10035742)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Social circumstances (10041244)	Sexual abuse (10040461)	0	0.0	0.0	0.7	1	0.1	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.5
Vascular disorders (10047065)	Kawasaki's disease (10023320)	1	0.2	0.0	1.1	0	0.0	0.0	0.5	0	0.0	0.0	0.7	0	0.0	0.0	0.5

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
6-17M = 6-17 months old subjects
18-35M = 18-35 months old subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 114 Incidence and nature of solicited AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by priming status (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	520	369	71.0	66.9	74.8	520	338	65.0	60.7	69.1	518	187	36.1	32.0	40.4
		PRIM	635	438	69.0	65.2	72.6	635	369	58.1	54.2	62.0	633	280	44.2	40.3	48.2
	F-QIV	UNPRIM	518	356	68.7	64.5	72.7	518	324	62.5	58.2	66.7	516	190	36.8	32.6	41.1
		PRIM	630	428	67.9	64.1	71.6	630	374	59.4	55.4	63.2	630	245	38.9	35.1	42.8
Dose 2	Q-QIV	UNPRIM	490	294	60.0	55.5	64.4	490	265	54.1	49.6	58.6	490	139	28.4	24.4	32.6
	F-QIV	UNPRIM	495	298	60.2	55.7	64.5	495	276	55.8	51.3	60.2	493	147	29.8	25.8	34.1
Overall/dose	Q-QIV	UNPRIM	1010	663	65.6	62.6	68.6	1010	603	59.7	56.6	62.7	1008	326	32.3	29.5	35.3
		PRIM	635	438	69.0	65.2	72.6	635	369	58.1	54.2	62.0	633	280	44.2	40.3	48.2
	F-QIV	UNPRIM	1013	654	64.6	61.5	67.5	1013	600	59.2	56.1	62.3	1009	337	33.4	30.5	36.4
		PRIM	630	428	67.9	64.1	71.6	630	374	59.4	55.4	63.2	630	245	38.9	35.1	42.8
Overall/subject	Q-QIV	UNPRIM	524	421	80.3	76.7	83.7	524	399	76.1	72.3	79.7	523	233	44.6	40.2	48.9
		PRIM	635	438	69.0	65.2	72.6	635	369	58.1	54.2	62.0	633	280	44.2	40.3	48.2
	F-QIV	UNPRIM	522	397	76.1	72.2	79.7	522	375	71.8	67.8	75.7	521	223	42.8	38.5	47.2
		PRIM	630	428	67.9	64.1	71.6	630	374	59.4	55.4	63.2	630	245	38.9	35.1	42.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 115 Incidence and nature of solicited grade 3 AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by priming status (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	520	48	9.2	6.9	12.1	520	42	8.1	5.9	10.8	518	12	2.3	1.2	4.0
		PRIM	635	51	8.0	6.0	10.4	635	40	6.3	4.5	8.5	633	16	2.5	1.5	4.1
	F-QIV	UNPRIM	518	39	7.5	5.4	10.1	518	36	6.9	4.9	9.5	516	11	2.1	1.1	3.8
		PRIM	630	39	6.2	4.4	8.4	630	35	5.6	3.9	7.6	630	5	0.8	0.3	1.8
Dose 2	Q-QIV	UNPRIM	490	40	8.2	5.9	11.0	490	34	6.9	4.9	9.6	490	9	1.8	0.8	3.5
	F-QIV	UNPRIM	495	24	4.8	3.1	7.1	495	22	4.4	2.8	6.7	493	3	0.6	0.1	1.8
Overall/dose	Q-QIV	UNPRIM	1010	88	8.7	7.0	10.6	1010	76	7.5	6.0	9.3	1008	21	2.1	1.3	3.2
		PRIM	635	51	8.0	6.0	10.4	635	40	6.3	4.5	8.5	633	16	2.5	1.5	4.1
	F-QIV	UNPRIM	1013	63	6.2	4.8	7.9	1013	58	5.7	4.4	7.3	1009	14	1.4	0.8	2.3
		PRIM	630	39	6.2	4.4	8.4	630	35	5.6	3.9	7.6	630	5	0.8	0.3	1.8
Overall/subject	Q-QIV	UNPRIM	524	77	14.7	11.8	18.0	524	69	13.2	10.4	16.4	523	18	3.4	2.1	5.4
		PRIM	635	51	8.0	6.0	10.4	635	40	6.3	4.5	8.5	633	16	2.5	1.5	4.1
	F-QIV	UNPRIM	522	54	10.3	7.9	13.3	522	49	9.4	7.0	12.2	521	14	2.7	1.5	4.5
		PRIM	630	39	6.2	4.4	8.4	630	35	5.6	3.9	7.6	630	5	0.8	0.3	1.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 116 Incidence and nature of solicited AEs with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by priming status (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	520	336	64.6	60.3	68.7	520	285	54.8	50.4	59.1	518	187	36.1	32.0	40.4
		PRIM	635	404	63.6	59.7	67.4	635	311	49.0	45.0	52.9	633	280	44.2	40.3	48.2
	F-QIV	UNPRIM	518	322	62.2	57.8	66.4	518	275	53.1	48.7	57.5	516	190	36.8	32.6	41.1
		PRIM	630	394	62.5	58.6	66.3	630	320	50.8	46.8	54.8	630	245	38.9	35.1	42.8
Dose 2	Q-QIV	UNPRIM	490	265	54.1	49.6	58.6	490	222	45.3	40.8	49.8	490	139	28.4	24.4	32.6
	F-QIV	UNPRIM	495	260	52.5	48.0	57.0	495	220	44.4	40.0	48.9	493	147	29.8	25.8	34.1
Overall/dose	Q-QIV	UNPRIM	1010	601	59.5	56.4	62.6	1010	507	50.2	47.1	53.3	1008	326	32.3	29.5	35.3
		PRIM	635	404	63.6	59.7	67.4	635	311	49.0	45.0	52.9	633	280	44.2	40.3	48.2
	F-QIV	UNPRIM	1013	582	57.5	54.3	60.5	1013	495	48.9	45.7	52.0	1009	337	33.4	30.5	36.4
		PRIM	630	394	62.5	58.6	66.3	630	320	50.8	46.8	54.8	630	245	38.9	35.1	42.8
Overall/subject	Q-QIV	UNPRIM	524	386	73.7	69.7	77.4	524	343	65.5	61.2	69.5	523	233	44.6	40.2	48.9
		PRIM	635	404	63.6	59.7	67.4	635	311	49.0	45.0	52.9	633	280	44.2	40.3	48.2
	F-QIV	UNPRIM	522	363	69.5	65.4	73.5	522	324	62.1	57.8	66.2	521	223	42.8	38.5	47.2
		PRIM	630	394	62.5	58.6	66.3	630	320	50.8	46.8	54.8	630	245	38.9	35.1	42.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 117 Incidence and nature of solicited grade 3 AEs with causal relationship to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by priming status (Total vaccinated cohort)

			Any symptom					General symptoms					Local symptoms				
						95% CI					95% CI					95% CI	
	Group	Sub-group	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Q-QIV	UNPRIM	520	41	7.9	5.7	10.5	520	32	6.2	4.2	8.6	518	12	2.3	1.2	4.0
		PRIM	635	45	7.1	5.2	9.4	635	33	5.2	3.6	7.2	633	16	2.5	1.5	4.1
	F-QIV	UNPRIM	518	37	7.1	5.1	9.7	518	34	6.6	4.6	9.1	516	11	2.1	1.1	3.8
		PRIM	630	33	5.2	3.6	7.3	630	29	4.6	3.1	6.5	630	5	0.8	0.3	1.8
Dose 2	Q-QIV	UNPRIM	490	32	6.5	4.5	9.1	490	26	5.3	3.5	7.7	490	9	1.8	0.8	3.5
	F-QIV	UNPRIM	495	14	2.8	1.6	4.7	495	12	2.4	1.3	4.2	493	3	0.6	0.1	1.8
Overall/dose	Q-QIV	UNPRIM	1010	73	7.2	5.7	9.0	1010	58	5.7	4.4	7.4	1008	21	2.1	1.3	3.2
		PRIM	635	45	7.1	5.2	9.4	635	33	5.2	3.6	7.2	633	16	2.5	1.5	4.1
	F-QIV	UNPRIM	1013	51	5.0	3.8	6.6	1013	46	4.5	3.3	6.0	1009	14	1.4	0.8	2.3
		PRIM	630	33	5.2	3.6	7.3	630	29	4.6	3.1	6.5	630	5	0.8	0.3	1.8
Overall/subject	Q-QIV	UNPRIM	524	64	12.2	9.5	15.3	524	53	10.1	7.7	13.0	523	18	3.4	2.1	5.4
		PRIM	635	45	7.1	5.2	9.4	635	33	5.2	3.6	7.2	633	16	2.5	1.5	4.1
	F-QIV	UNPRIM	522	46	8.8	6.5	11.6	522	41	7.9	5.7	10.5	521	14	2.7	1.5	4.5
		PRIM	630	33	5.2	3.6	7.3	630	29	4.6	3.1	6.5	630	5	0.8	0.3	1.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 118 Incidence of solicited local AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by priming status (Total vaccinated cohort)

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																					
Pain	All	518	187	36.1	32.0	40.4	633	277	43.8	39.9	47.7	516	190	36.8	32.6	41.1	630	239	37.9	34.1	41.9
	Grade 2 or 3	518	59	11.4	8.8	14.4	633	91	14.4	11.7	17.4	516	55	10.7	8.1	13.6	630	72	11.4	9.1	14.2
	Grade 3	518	12	2.3	1.2	4.0	633	16	2.5	1.5	4.1	516	11	2.1	1.1	3.8	630	5	0.8	0.3	1.8
	Medical advice	518	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	516	1	0.2	0.0	1.1	630	2	0.3	0.0	1.1
Redness (mm)	All	518	2	0.4	0.0	1.4	633	13	2.1	1.1	3.5	516	2	0.4	0.0	1.4	630	13	2.1	1.1	3.5
	>50	518	0	0.0	0.0	0.7	633	5	0.8	0.3	1.8	516	1	0.2	0.0	1.1	630	3	0.5	0.1	1.4
	>100	518	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	516	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Medical advice	518	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	516	0	0.0	0.0	0.7	630	2	0.3	0.0	1.1
Swelling (mm)	All	518	4	0.8	0.2	2.0	633	7	1.1	0.4	2.3	516	0	0.0	0.0	0.7	630	5	0.8	0.3	1.8
	>50	518	1	0.2	0.0	1.1	633	1	0.2	0.0	0.9	516	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	>100	518	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	516	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Medical advice	518	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	516	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
Dose 2																					
Pain	All	490	138	28.2	24.2	32.4						493	147	29.8	25.8	34.1					
	Grade 2 or 3	490	31	6.3	4.3	8.9						493	36	7.3	5.2	10.0					
	Grade 3	490	9	1.8	0.8	3.5						493	3	0.6	0.1	1.8					
	Medical advice	490	0	0.0	0.0	0.8						493	0	0.0	0.0	0.7					
Redness (mm)	All	490	1	0.2	0.0	1.1						493	2	0.4	0.0	1.5					
	>50	490	0	0.0	0.0	0.8						493	0	0.0	0.0	0.7					
	>100	490	0	0.0	0.0	0.8						493	0	0.0	0.0	0.7					
	Medical advice	490	1	0.2	0.0	1.1						493	0	0.0	0.0	0.7					
Swelling (mm)	All	490	0	0.0	0.0	0.8						493	0	0.0	0.0	0.7					
	>50	490	0	0.0	0.0	0.8						493	0	0.0	0.0	0.7					
	>100	490	0	0.0	0.0	0.8						493	0	0.0	0.0	0.7					
	Medical advice	490	0	0.0	0.0	0.8						493	0	0.0	0.0	0.7					
Overall/dose																					
Pain	All	1008	325	32.2	29.4	35.2	633	277	43.8	39.9	47.7	1009	337	33.4	30.5	36.4	630	239	37.9	34.1	41.9
	Grade 2 or 3	1008	90	8.9	7.2	10.9	633	91	14.4	11.7	17.4	1009	91	9.0	7.3	11.0	630	72	11.4	9.1	14.2
	Grade 3	1008	21	2.1	1.3	3.2	633	16	2.5	1.5	4.1	1009	14	1.4	0.8	2.3	630	5	0.8	0.3	1.8
	Medical advice	1008	0	0.0	0.0	0.4	633	0	0.0	0.0	0.6	1009	1	0.1	0.0	0.6	630	2	0.3	0.0	1.1

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI				95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Redness (mm)	All	1008	3	0.3	0.1	0.9	633	13	2.1	1.1	3.5	1009	4	0.4	0.1	1.0	630	13	2.1	1.1	3.5
	>50	1008	0	0.0	0.0	0.4	633	5	0.8	0.3	1.8	1009	1	0.1	0.0	0.6	630	3	0.5	0.1	1.4
	>100	1008	0	0.0	0.0	0.4	633	0	0.0	0.0	0.6	1009	0	0.0	0.0	0.4	630	0	0.0	0.0	0.6
	Medical advice	1008	1	0.1	0.0	0.6	633	0	0.0	0.0	0.6	1009	0	0.0	0.0	0.4	630	2	0.3	0.0	1.1
Swelling (mm)	All	1008	4	0.4	0.1	1.0	633	7	1.1	0.4	2.3	1009	0	0.0	0.0	0.4	630	5	0.8	0.3	1.8
	>50	1008	1	0.1	0.0	0.6	633	1	0.2	0.0	0.9	1009	0	0.0	0.0	0.4	630	0	0.0	0.0	0.6
	>100	1008	0	0.0	0.0	0.4	633	0	0.0	0.0	0.6	1009	0	0.0	0.0	0.4	630	0	0.0	0.0	0.6
	Medical advice	1008	0	0.0	0.0	0.4	633	0	0.0	0.0	0.6	1009	0	0.0	0.0	0.4	630	0	0.0	0.0	0.6
Overall/subject																					
Pain	All	523	232	44.4	40.0	48.7	633	277	43.8	39.9	47.7	521	223	42.8	38.5	47.2	630	239	37.9	34.1	41.9
	Grade 2 or 3	523	73	14.0	11.1	17.2	633	91	14.4	11.7	17.4	521	78	15.0	12.0	18.3	630	72	11.4	9.1	14.2
	Grade 3	523	18	3.4	2.1	5.4	633	16	2.5	1.5	4.1	521	14	2.7	1.5	4.5	630	5	0.8	0.3	1.8
	Medical advice	523	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	521	1	0.2	0.0	1.1	630	2	0.3	0.0	1.1
Redness (mm)	All	523	3	0.6	0.1	1.7	633	13	2.1	1.1	3.5	521	3	0.6	0.1	1.7	630	13	2.1	1.1	3.5
	>50	523	0	0.0	0.0	0.7	633	5	0.8	0.3	1.8	521	1	0.2	0.0	1.1	630	3	0.5	0.1	1.4
	>100	523	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	521	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Medical advice	523	1	0.2	0.0	1.1	633	0	0.0	0.0	0.6	521	0	0.0	0.0	0.7	630	2	0.3	0.0	1.1
Swelling (mm)	All	523	4	0.8	0.2	1.9	633	7	1.1	0.4	2.3	521	0	0.0	0.0	0.7	630	5	0.8	0.3	1.8
	>50	523	1	0.2	0.0	1.1	633	1	0.2	0.0	0.9	521	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	>100	523	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	521	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Medical advice	523	0	0.0	0.0	0.7	633	0	0.0	0.0	0.6	521	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 119 Incidence of solicited general AEs reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall by priming status (Total vaccinated cohort)

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1																					
Drowsiness	All	520	212	40.8	36.5	45.1	635	212	33.4	29.7	37.2	518	211	40.7	36.5	45.1	630	213	33.8	30.1	37.7
	Grade 2 or 3	520	65	12.5	9.8	15.7	635	67	10.6	8.3	13.2	518	73	14.1	11.2	17.4	630	70	11.1	8.8	13.8
	Grade 3	520	15	2.9	1.6	4.7	635	16	2.5	1.4	4.1	518	19	3.7	2.2	5.7	630	11	1.7	0.9	3.1
	Related	520	182	35.0	30.9	39.3	635	183	28.8	25.3	32.5	518	189	36.5	32.3	40.8	630	192	30.5	26.9	34.2
	Grade 3 Related	520	14	2.7	1.5	4.5	635	13	2.0	1.1	3.5	518	18	3.5	2.1	5.4	630	10	1.6	0.8	2.9
	Medical advice	520	10	1.9	0.9	3.5	635	2	0.3	0.0	1.1	518	1	0.2	0.0	1.1	630	6	1.0	0.4	2.1
Fever/(Axillary) (°C)	All	520	80	15.4	12.4	18.8	635	66	10.4	8.1	13.0	518	69	13.3	10.5	16.6	630	78	12.4	9.9	15.2
	≥38	520	41	7.9	5.7	10.5	635	24	3.8	2.4	5.6	518	33	6.4	4.4	8.8	630	34	5.4	3.8	7.5
	>38.5	520	24	4.6	3.0	6.8	635	9	1.4	0.7	2.7	518	12	2.3	1.2	4.0	630	18	2.9	1.7	4.5
	>39.0	520	12	2.3	1.2	4.0	635	4	0.6	0.2	1.6	518	3	0.6	0.1	1.7	630	8	1.3	0.5	2.5
	>39.5	520	9	1.7	0.8	3.3	635	2	0.3	0.0	1.1	518	2	0.4	0.0	1.4	630	2	0.3	0.0	1.1
	>40.0	520	2	0.4	0.0	1.4	635	0	0.0	0.0	0.6	518	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Related	520	24	4.6	3.0	6.8	635	17	2.7	1.6	4.3	518	25	4.8	3.1	7.0	630	25	4.0	2.6	5.8
	≥38 Related	520	24	4.6	3.0	6.8	635	17	2.7	1.6	4.3	518	25	4.8	3.1	7.0	630	25	4.0	2.6	5.8
	>38.5 Related	520	11	2.1	1.1	3.8	635	5	0.8	0.3	1.8	518	9	1.7	0.8	3.3	630	10	1.6	0.8	2.9
	>39.0 Related	520	5	1.0	0.3	2.2	635	3	0.5	0.1	1.4	518	3	0.6	0.1	1.7	630	3	0.5	0.1	1.4
	>39.5 Related	520	3	0.6	0.1	1.7	635	1	0.2	0.0	0.9	518	2	0.4	0.0	1.4	630	1	0.2	0.0	0.9
	>40.0 Related	520	0	0.0	0.0	0.7	635	0	0.0	0.0	0.6	518	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Medical advice	520	14	2.7	1.5	4.5	635	3	0.5	0.1	1.4	518	5	1.0	0.3	2.2	630	5	0.8	0.3	1.8

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Irritability / Fussiness	All	520	274	52.7	48.3	57.1	635	296	46.6	42.7	50.6	518	256	49.4	45.0	53.8	630	271	43.0	39.1	47.0
	Grade 2 or 3	520	107	20.6	17.2	24.3	635	117	18.4	15.5	21.7	518	95	18.3	15.1	21.9	630	97	15.4	12.7	18.5
	Grade 3	520	21	4.0	2.5	6.1	635	23	3.6	2.3	5.4	518	14	2.7	1.5	4.5	630	20	3.2	1.9	4.9
	Related	520	240	46.2	41.8	50.5	635	259	40.8	36.9	44.7	518	227	43.8	39.5	48.2	630	246	39.0	35.2	43.0
	Grade 3 Related	520	18	3.5	2.1	5.4	635	19	3.0	1.8	4.6	518	14	2.7	1.5	4.5	630	19	3.0	1.8	4.7
	Medical advice	520	12	2.3	1.2	4.0	635	5	0.8	0.3	1.8	518	3	0.6	0.1	1.7	630	9	1.4	0.7	2.7
Loss Of Appetite	All	520	154	29.6	25.7	33.7	635	180	28.3	24.9	32.0	518	138	26.6	22.9	30.7	630	190	30.2	26.6	33.9
	Grade 2 or 3	520	37	7.1	5.1	9.7	635	46	7.2	5.4	9.5	518	42	8.1	5.9	10.8	630	50	7.9	5.9	10.3
	Grade 3	520	7	1.3	0.5	2.8	635	12	1.9	1.0	3.3	518	6	1.2	0.4	2.5	630	9	1.4	0.7	2.7
	Related	520	129	24.8	21.2	28.8	635	151	23.8	20.5	27.3	518	119	23.0	19.4	26.8	630	171	27.1	23.7	30.8
	Grade 3 Related	520	7	1.3	0.5	2.8	635	9	1.4	0.7	2.7	518	5	1.0	0.3	2.2	630	9	1.4	0.7	2.7
	Medical advice	520	10	1.9	0.9	3.5	635	4	0.6	0.2	1.6	518	3	0.6	0.1	1.7	630	6	1.0	0.4	2.1
Dose 2																					
Drowsiness	All	490	157	32.0	27.9	36.4						495	166	33.5	29.4	37.9					
	Grade 2 or 3	490	43	8.8	6.4	11.6						495	53	10.7	8.1	13.8					
	Grade 3	490	10	2.0	1.0	3.7						495	6	1.2	0.4	2.6					
	Related	490	133	27.1	23.3	31.3						495	136	27.5	23.6	31.6					
	Grade 3 Related	490	6	1.2	0.5	2.6						495	2	0.4	0.0	1.5					
	Medical advice	490	5	1.0	0.3	2.4						495	6	1.2	0.4	2.6					
Fever/(Axillary) (°C)	All	490	60	12.2	9.5	15.5						495	48	9.7	7.2	12.7					
	≥38	490	31	6.3	4.3	8.9						495	22	4.4	2.8	6.7					
	>38.5	490	17	3.5	2.0	5.5						495	11	2.2	1.1	3.9					
	>39.0	490	9	1.8	0.8	3.5						495	6	1.2	0.4	2.6					

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
	>39.5	490	4	0.8	0.2	2.1						495	1	0.2	0.0	1.1					
	>40.0	490	3	0.6	0.1	1.8						495	0	0.0	0.0	0.7					
	Related	490	22	4.5	2.8	6.7						495	14	2.8	1.6	4.7					
	≥38 Related	490	20	4.1	2.5	6.2						495	13	2.6	1.4	4.4					
	>38.5 Related	490	12	2.4	1.3	4.2						495	5	1.0	0.3	2.3					
	>39.0 Related	490	6	1.2	0.5	2.6						495	2	0.4	0.0	1.5					
	>39.5 Related	490	2	0.4	0.0	1.5						495	0	0.0	0.0	0.7					
	>40.0 Related	490	1	0.2	0.0	1.1						495	0	0.0	0.0	0.7					
	Medical advice	490	9	1.8	0.8	3.5						495	7	1.4	0.6	2.9					
Irritability / Fussiness	All	490	211	43.1	38.6	47.6						495	214	43.2	38.8	47.7					
	Grade 2 or 3	490	75	15.3	12.2	18.8						495	71	14.3	11.4	17.7					
	Grade 3	490	21	4.3	2.7	6.5						495	14	2.8	1.6	4.7					
	Related	490	185	37.8	33.4	42.2						495	175	35.4	31.1	39.7					
	Grade 3 Related	490	18	3.7	2.2	5.7						495	9	1.8	0.8	3.4					
	Medical advice	490	7	1.4	0.6	2.9						495	11	2.2	1.1	3.9					
Loss Of Appetite	All	490	110	22.4	18.8	26.4						495	116	23.4	19.8	27.4					
	Grade 2 or 3	490	32	6.5	4.5	9.1						495	29	5.9	4.0	8.3					
	Grade 3	490	8	1.6	0.7	3.2						495	5	1.0	0.3	2.3					
	Related	490	91	18.6	15.2	22.3						495	87	17.6	14.3	21.2					
	Grade 3 Related	490	4	0.8	0.2	2.1						495	2	0.4	0.0	1.5					
	Medical advice	490	5	1.0	0.3	2.4						495	11	2.2	1.1	3.9					

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Overall/dose																					
Drowsiness	All	1010	369	36.5	33.6	39.6	635	212	33.4	29.7	37.2	1013	377	37.2	34.2	40.3	630	213	33.8	30.1	37.7
	Grade 2 or 3	1010	108	10.7	8.9	12.8	635	67	10.6	8.3	13.2	1013	126	12.4	10.5	14.6	630	70	11.1	8.8	13.8
	Grade 3	1010	25	2.5	1.6	3.6	635	16	2.5	1.4	4.1	1013	25	2.5	1.6	3.6	630	11	1.7	0.9	3.1
	Related	1010	315	31.2	28.3	34.1	635	183	28.8	25.3	32.5	1013	325	32.1	29.2	35.1	630	192	30.5	26.9	34.2
	Grade 3 Related	1010	20	2.0	1.2	3.0	635	13	2.0	1.1	3.5	1013	20	2.0	1.2	3.0	630	10	1.6	0.8	2.9
	Medical advice	1010	15	1.5	0.8	2.4	635	2	0.3	0.0	1.1	1013	7	0.7	0.3	1.4	630	6	1.0	0.4	2.1
Fever/(Axillary) (°C)	All	1010	140	13.9	11.8	16.1	635	66	10.4	8.1	13.0	1013	117	11.5	9.6	13.7	630	78	12.4	9.9	15.2
	≥38	1010	72	7.1	5.6	8.9	635	24	3.8	2.4	5.6	1013	55	5.4	4.1	7.0	630	34	5.4	3.8	7.5
	>38.5	1010	41	4.1	2.9	5.5	635	9	1.4	0.7	2.7	1013	23	2.3	1.4	3.4	630	18	2.9	1.7	4.5
	>39.0	1010	21	2.1	1.3	3.2	635	4	0.6	0.2	1.6	1013	9	0.9	0.4	1.7	630	8	1.3	0.5	2.5
	>39.5	1010	13	1.3	0.7	2.2	635	2	0.3	0.0	1.1	1013	3	0.3	0.1	0.9	630	2	0.3	0.0	1.1
	>40.0	1010	5	0.5	0.2	1.2	635	0	0.0	0.0	0.6	1013	0	0.0	0.0	0.4	630	0	0.0	0.0	0.6
	Related	1010	46	4.6	3.4	6.0	635	17	2.7	1.6	4.3	1013	39	3.8	2.8	5.2	630	25	4.0	2.6	5.8
	≥38 Related	1010	44	4.4	3.2	5.8	635	17	2.7	1.6	4.3	1013	38	3.8	2.7	5.1	630	25	4.0	2.6	5.8
	>38.5 Related	1010	23	2.3	1.4	3.4	635	5	0.8	0.3	1.8	1013	14	1.4	0.8	2.3	630	10	1.6	0.8	2.9
	>39.0 Related	1010	11	1.1	0.5	1.9	635	3	0.5	0.1	1.4	1013	5	0.5	0.2	1.1	630	3	0.5	0.1	1.4
	>39.5 Related	1010	5	0.5	0.2	1.2	635	1	0.2	0.0	0.9	1013	2	0.2	0.0	0.7	630	1	0.2	0.0	0.9
	>40.0 Related	1010	1	0.1	0.0	0.6	635	0	0.0	0.0	0.6	1013	0	0.0	0.0	0.4	630	0	0.0	0.0	0.6
	Medical advice	1010	23	2.3	1.4	3.4	635	3	0.5	0.1	1.4	1013	12	1.2	0.6	2.1	630	5	0.8	0.3	1.8
Irritability / Fussiness	All	1010	485	48.0	44.9	51.2	635	296	46.6	42.7	50.6	1013	470	46.4	43.3	49.5	630	271	43.0	39.1	47.0
	Grade 2 or 3	1010	182	18.0	15.7	20.5	635	117	18.4	15.5	21.7	1013	166	16.4	14.2	18.8	630	97	15.4	12.7	18.5

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Grade 3	1010	42	4.2	3.0	5.6	635	23	3.6	2.3	5.4	1013	28	2.8	1.8	4.0	630	20	3.2	1.9	4.9
	Related	1010	425	42.1	39.0	45.2	635	259	40.8	36.9	44.7	1013	402	39.7	36.7	42.8	630	246	39.0	35.2	43.0
	Grade 3 Related	1010	36	3.6	2.5	4.9	635	19	3.0	1.8	4.6	1013	23	2.3	1.4	3.4	630	19	3.0	1.8	4.7
	Medical advice	1010	19	1.9	1.1	2.9	635	5	0.8	0.3	1.8	1013	14	1.4	0.8	2.3	630	9	1.4	0.7	2.7
Loss Of Appetite	All	1010	264	26.1	23.5	29.0	635	180	28.3	24.9	32.0	1013	254	25.1	22.4	27.9	630	190	30.2	26.6	33.9
	Grade 2 or 3	1010	69	6.8	5.4	8.6	635	46	7.2	5.4	9.5	1013	71	7.0	5.5	8.8	630	50	7.9	5.9	10.3
	Grade 3	1010	15	1.5	0.8	2.4	635	12	1.9	1.0	3.3	1013	11	1.1	0.5	1.9	630	9	1.4	0.7	2.7
	Related	1010	220	21.8	19.3	24.5	635	151	23.8	20.5	27.3	1013	206	20.3	17.9	22.9	630	171	27.1	23.7	30.8
	Grade 3 Related	1010	11	1.1	0.5	1.9	635	9	1.4	0.7	2.7	1013	7	0.7	0.3	1.4	630	9	1.4	0.7	2.7
	Medical advice	1010	15	1.5	0.8	2.4	635	4	0.6	0.2	1.6	1013	14	1.4	0.8	2.3	630	6	1.0	0.4	2.1
Overall/subject																					
Drowsiness	All	524	259	49.4	45.1	53.8	635	212	33.4	29.7	37.2	522	258	49.4	45.1	53.8	630	213	33.8	30.1	37.7
	Grade 2 or 3	524	93	17.7	14.6	21.3	635	67	10.6	8.3	13.2	522	107	20.5	17.1	24.2	630	70	11.1	8.8	13.8
	Grade 3	524	20	3.8	2.3	5.8	635	16	2.5	1.4	4.1	522	23	4.4	2.8	6.5	630	11	1.7	0.9	3.1
	Related	524	228	43.5	39.2	47.9	635	183	28.8	25.3	32.5	522	233	44.6	40.3	49.0	630	192	30.5	26.9	34.2
	Grade 3 Related	524	16	3.1	1.8	4.9	635	13	2.0	1.1	3.5	522	19	3.6	2.2	5.6	630	10	1.6	0.8	2.9
	Medical advice	524	13	2.5	1.3	4.2	635	2	0.3	0.0	1.1	522	7	1.3	0.5	2.7	630	6	1.0	0.4	2.1
Fever/(Axillary) (°C)	All	524	117	22.3	18.8	26.1	635	66	10.4	8.1	13.0	522	100	19.2	15.9	22.8	630	78	12.4	9.9	15.2
	≥38	524	67	12.8	10.0	16.0	635	24	3.8	2.4	5.6	522	52	10.0	7.5	12.9	630	34	5.4	3.8	7.5
	>38.5	524	39	7.4	5.3	10.0	635	9	1.4	0.7	2.7	522	23	4.4	2.8	6.5	630	18	2.9	1.7	4.5
	>39.0	524	21	4.0	2.5	6.1	635	4	0.6	0.2	1.6	522	9	1.7	0.8	3.2	630	8	1.3	0.5	2.5
	>39.5	524	13	2.5	1.3	4.2	635	2	0.3	0.0	1.1	522	3	0.6	0.1	1.7	630	2	0.3	0.0	1.1
	>40.0	524	5	1.0	0.3	2.2	635	0	0.0	0.0	0.6	522	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Related	524	45	8.6	6.3	11.3	635	17	2.7	1.6	4.3	522	38	7.3	5.2	9.9	630	25	4.0	2.6	5.8

		Q-QIV										F-QIV									
		UNPRIM					PRIM					UNPRIM					PRIM				
					95 % CI					95 % CI					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
	≥38 Related	524	43	8.2	6.0	10.9	635	17	2.7	1.6	4.3	522	37	7.1	5.0	9.6	630	25	4.0	2.6	5.8
	>38.5 Related	524	23	4.4	2.8	6.5	635	5	0.8	0.3	1.8	522	14	2.7	1.5	4.5	630	10	1.6	0.8	2.9
	>39.0 Related	524	11	2.1	1.1	3.7	635	3	0.5	0.1	1.4	522	5	1.0	0.3	2.2	630	3	0.5	0.1	1.4
	>39.5 Related	524	5	1.0	0.3	2.2	635	1	0.2	0.0	0.9	522	2	0.4	0.0	1.4	630	1	0.2	0.0	0.9
	>40.0 Related	524	1	0.2	0.0	1.1	635	0	0.0	0.0	0.6	522	0	0.0	0.0	0.7	630	0	0.0	0.0	0.6
	Medical advice	524	21	4.0	2.5	6.1	635	3	0.5	0.1	1.4	522	12	2.3	1.2	4.0	630	5	0.8	0.3	1.8
Irritability / Fussiness	All	524	334	63.7	59.5	67.9	635	296	46.6	42.7	50.6	522	311	59.6	55.2	63.8	630	271	43.0	39.1	47.0
	Grade 2 or 3	524	148	28.2	24.4	32.3	635	117	18.4	15.5	21.7	522	132	25.3	21.6	29.2	630	97	15.4	12.7	18.5
	Grade 3	524	38	7.3	5.2	9.8	635	23	3.6	2.3	5.4	522	25	4.8	3.1	7.0	630	20	3.2	1.9	4.9
	Related	524	299	57.1	52.7	61.3	635	259	40.8	36.9	44.7	522	279	53.4	49.1	57.8	630	246	39.0	35.2	43.0
	Grade 3 Related	524	33	6.3	4.4	8.7	635	19	3.0	1.8	4.6	522	20	3.8	2.4	5.9	630	19	3.0	1.8	4.7
	Medical advice	524	18	3.4	2.0	5.4	635	5	0.8	0.3	1.8	522	13	2.5	1.3	4.2	630	9	1.4	0.7	2.7
Loss Of Appetite	All	524	211	40.3	36.0	44.6	635	180	28.3	24.9	32.0	522	195	37.4	33.2	41.7	630	190	30.2	26.6	33.9
	Grade 2 or 3	524	63	12.0	9.4	15.1	635	46	7.2	5.4	9.5	522	62	11.9	9.2	15.0	630	50	7.9	5.9	10.3
	Grade 3	524	14	2.7	1.5	4.4	635	12	1.9	1.0	3.3	522	10	1.9	0.9	3.5	630	9	1.4	0.7	2.7
	Related	524	177	33.8	29.7	38.0	635	151	23.8	20.5	27.3	522	166	31.8	27.8	36.0	630	171	27.1	23.7	30.8
	Grade 3 Related	524	10	1.9	0.9	3.5	635	9	1.4	0.7	2.7	522	7	1.3	0.5	2.7	630	9	1.4	0.7	2.7
	Medical advice	524	13	2.5	1.3	4.2	635	4	0.6	0.2	1.6	522	13	2.5	1.3	4.2	630	6	1.0	0.4	2.1

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects

PRIM = Primed subjects
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
For Overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Table 120 Number of days with solicited local and general AEs during the 7-day follow-up period by priming status (Total vaccinated cohort)

Solicited symptom	Dose	Group	Sub-group	N	Mean	Min	Q1	Median	Q3	Max
Drowsiness	Dose 1	Q-QIV	UNPRIM	212	2.0	1.0	1.0	2.0	2.0	7.0
			PRIM	212	1.9	1.0	1.0	1.0	2.0	7.0
		F-QIV	UNPRIM	211	2.0	1.0	1.0	2.0	3.0	7.0
			PRIM	213	2.0	1.0	1.0	1.0	2.0	7.0
	Dose 2	Q-QIV	UNPRIM	157	2.0	1.0	1.0	2.0	2.0	7.0
		F-QIV	UNPRIM	166	2.1	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	UNPRIM	369	2.0	1.0	1.0	2.0	2.0	7.0
			PRIM	212	1.9	1.0	1.0	1.0	2.0	7.0
		F-QIV	UNPRIM	377	2.1	1.0	1.0	2.0	3.0	7.0
			PRIM	213	2.0	1.0	1.0	1.0	2.0	7.0
Irritability / fussiness	Dose 1	Q-QIV	UNPRIM	274	2.4	1.0	1.0	2.0	3.0	7.0
			PRIM	296	2.3	1.0	1.0	2.0	3.0	7.0
		F-QIV	UNPRIM	256	2.5	1.0	1.0	2.0	3.0	7.0
			PRIM	271	2.4	1.0	1.0	2.0	3.0	7.0
	Dose 2	Q-QIV	UNPRIM	211	2.5	1.0	1.0	2.0	3.0	7.0
		F-QIV	UNPRIM	214	2.3	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	UNPRIM	485	2.5	1.0	1.0	2.0	3.0	7.0
			PRIM	296	2.3	1.0	1.0	2.0	3.0	7.0
		F-QIV	UNPRIM	470	2.5	1.0	1.0	2.0	3.0	7.0
			PRIM	271	2.4	1.0	1.0	2.0	3.0	7.0
Loss of appetite	Dose 1	Q-QIV	UNPRIM	154	2.4	1.0	1.0	2.0	3.0	7.0
			PRIM	180	2.1	1.0	1.0	1.0	3.0	7.0
		F-QIV	UNPRIM	138	2.4	1.0	1.0	2.0	3.0	7.0
			PRIM	190	2.2	1.0	1.0	2.0	3.0	7.0
	Dose 2	Q-QIV	UNPRIM	110	2.5	1.0	1.0	2.0	3.0	7.0
		F-QIV	UNPRIM	116	2.2	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	UNPRIM	264	2.4	1.0	1.0	2.0	3.0	7.0
			PRIM	180	2.1	1.0	1.0	1.0	3.0	7.0
		F-QIV	UNPRIM	254	2.3	1.0	1.0	2.0	3.0	7.0
			PRIM	190	2.2	1.0	1.0	2.0	3.0	7.0
Pain	Dose 1	Q-QIV	UNPRIM	187	1.8	1.0	1.0	1.0	2.0	7.0
			PRIM	277	1.8	1.0	1.0	2.0	2.0	7.0
		F-QIV	UNPRIM	190	1.8	1.0	1.0	1.0	2.0	6.0
			PRIM	239	1.9	1.0	1.0	2.0	2.0	6.0
	Dose 2	Q-QIV	UNPRIM	138	1.7	1.0	1.0	1.0	2.0	6.0
		F-QIV	UNPRIM	147	1.7	1.0	1.0	1.0	2.0	5.0
	Overall/dose	Q-QIV	UNPRIM	325	1.8	1.0	1.0	1.0	2.0	7.0
			PRIM	277	1.8	1.0	1.0	2.0	2.0	7.0
		F-QIV	UNPRIM	337	1.7	1.0	1.0	1.0	2.0	6.0
			PRIM	239	1.9	1.0	1.0	2.0	2.0	6.0
Redness	Dose 1	Q-QIV	UNPRIM	2	1.5	1.0	1.0	1.5	2.0	2.0
			PRIM	13	2.1	1.0	1.0	2.0	3.0	4.0
		F-QIV	UNPRIM	2	2.0	1.0	1.0	2.0	3.0	3.0
			PRIM	13	2.1	1.0	1.0	1.0	2.0	6.0
	Dose 2	Q-QIV	UNPRIM	1	1.0	1.0	1.0	1.0	1.0	1.0
		F-QIV	UNPRIM	2	1.5	1.0	1.0	1.5	2.0	2.0
	Overall/dose	Q-QIV	UNPRIM	3	1.3	1.0	1.0	1.0	2.0	2.0
			PRIM	13	2.1	1.0	1.0	2.0	3.0	4.0
		F-QIV	UNPRIM	4	1.8	1.0	1.0	1.5	2.5	3.0
			PRIM	13	2.1	1.0	1.0	1.0	2.0	6.0

Solicited symptom	Dose	Group	Sub-group	N	Mean	Min	Q1	Median	Q3	Max
Swelling	Dose 1	Q-QIV	UNPRIM	4	1.5	1.0	1.0	1.5	2.0	2.0
			PRIM	7	2.9	1.0	2.0	2.0	5.0	5.0
		F-QIV	PRIM	5	1.8	1.0	1.0	2.0	2.0	3.0
	Overall/dose	Q-QIV	UNPRIM	4	1.5	1.0	1.0	1.5	2.0	2.0
			PRIM	7	2.9	1.0	2.0	2.0	5.0	5.0
		F-QIV	PRIM	5	1.8	1.0	1.0	2.0	2.0	3.0
Fever	Dose 1	Q-QIV	UNPRIM	80	2.1	1.0	1.0	1.0	2.0	7.0
			PRIM	66	2.0	1.0	1.0	1.0	2.0	7.0
		F-QIV	UNPRIM	69	2.0	1.0	1.0	1.0	3.0	7.0
			PRIM	78	1.7	1.0	1.0	1.0	2.0	6.0
	Dose 2	Q-QIV	UNPRIM	60	1.8	1.0	1.0	1.0	2.0	7.0
		F-QIV	UNPRIM	48	2.1	1.0	1.0	2.0	3.0	7.0
	Overall/dose	Q-QIV	UNPRIM	140	1.9	1.0	1.0	1.0	2.0	7.0
			PRIM	66	2.0	1.0	1.0	1.0	2.0	7.0
		F-QIV	UNPRIM	117	2.0	1.0	1.0	1.0	3.0	7.0
			PRIM	78	1.7	1.0	1.0	1.0	2.0	6.0

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
N = number of doses with the symptom
Q1 = 25th percentile
Q3 = 75th percentile

Table 121 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		310	56.4	52.1	60.6	239	36.4	32.7	40.2	302	53.9	49.7	58.1	235	35.8	32.1	39.6
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Iron deficiency anaemia (10022972)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Leukocytosis (10024378)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Lymphadenopathy (10025197)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Neutropenia (10029354)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Congenital, familial and genetic disorders (10010331)	Phimosis (10034878)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Tibial torsion (10064515)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	3	0.5	0.1	1.6	2	0.3	0.0	1.1
	Ear discomfort (10052137)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Ear pain (10014020)	2	0.4	0.0	1.3	4	0.6	0.2	1.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Middle ear effusion (10062545)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dacryostenosis acquired (10053990)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Eye discharge (10015915)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Eye pruritus (10052140)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Eyelid oedema (10015993)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Lacrimation increased (10023644)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Photophobia (10034960)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Gastrointestinal disorders (10017947)	Abdominal discomfort (10000059)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Abdominal hernia (10060954)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Abdominal pain upper (10000087)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Constipation (10010774)	4	0.7	0.2	1.9	1	0.2	0.0	0.8	4	0.7	0.2	1.8	1	0.2	0.0	0.8

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Dental caries (10012318)	0	0.0	0.0	0.7	3	0.5	0.1	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Diarrhoea (10012735)	39	7.1	5.1	9.6	27	4.1	2.7	5.9	21	3.8	2.3	5.7	32	4.9	3.4	6.8
	Faeces hard (10016101)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Flatulence (10016766)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Food poisoning (10016952)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Frequent bowel movements (10017367)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Haematochezia (10018836)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Nausea (10028813)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Regurgitation (10067171)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Stomatitis (10042128)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Teething (10043183)	13	2.4	1.3	4.0	2	0.3	0.0	1.1	16	2.9	1.6	4.6	5	0.8	0.2	1.8
	Vomiting (10047700)	30	5.5	3.7	7.7	17	2.6	1.5	4.1	21	3.8	2.3	5.7	25	3.8	2.5	5.6
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Administration site rash (10071156)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Asthenia (10003549)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Chills (10008531)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Developmental delay (10012559)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Discomfort (10013082)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Fatigue (10016256)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Feeling hot (10016334)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Ill-defined disorder (10061520)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Influenza like illness (10022004)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Injection site bruising (10022052)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Injection site pruritus (10022093)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Injection site rash (10022094)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Injection site warmth (10022112)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Local swelling (10024770)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Malaise (10025482)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pain (10033371)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pyrexia (10037660)	26	4.7	3.1	6.9	28	4.3	2.9	6.1	36	6.4	4.5	8.8	20	3.0	1.9	4.7
	Thirst (10043458)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Vaccination site pain (10068879)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Vaccination site rash (10069482)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Vaccination site reaction (10059080)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Vaccination site swelling (10069620)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Vessel puncture site haemorrhage (10054092)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Immune system disorders (10021428)	Drug hypersensitivity (10013700)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Hypersensitivity (10020751)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Multiple allergies (10028164)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Seasonal allergy (10048908)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Acarodermatitis (10063409)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Acute sinusitis (10001076)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	3	0.5	0.1	1.6	2	0.3	0.0	1.1
	Bronchiolitis (10006448)	9	1.6	0.8	3.1	0	0.0	0.0	0.6	15	2.7	1.5	4.4	1	0.2	0.0	0.8
	Bronchitis (10006451)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	7	1.3	0.5	2.6	2	0.3	0.0	1.1
	Candida infection (10074170)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	3	0.5	0.1	1.6	0	0.0	0.0	0.6
	Candida nappy rash (10007135)	4	0.7	0.2	1.9	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Cellulitis (10007882)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Clostridium difficile infection (10054236)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Conjunctivitis (10010741)	9	1.6	0.8	3.1	4	0.6	0.2	1.6	13	2.3	1.2	3.9	7	1.1	0.4	2.2
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Coxsackie viral infection (10011261)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Croup infectious (10011416)	7	1.3	0.5	2.6	8	1.2	0.5	2.4	9	1.6	0.7	3.0	5	0.8	0.2	1.8
	Dermatophytosis (10012504)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Ear infection (10014011)	7	1.3	0.5	2.6	3	0.5	0.1	1.3	9	1.6	0.7	3.0	2	0.3	0.0	1.1
	Enterobiasis (10014881)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Exanthema subitum (10015586)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Eye infection (10015929)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Folliculitis (10016936)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Fungal infection (10017533)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Fungal skin infection (10017543)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Gastroenteritis (10017888)	7	1.3	0.5	2.6	7	1.1	0.4	2.2	17	3.0	1.8	4.8	5	0.8	0.2	1.8
	Gastroenteritis viral (10017918)	3	0.5	0.1	1.6	1	0.2	0.0	0.8	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Genital candidiasis (10018143)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Groin abscess (10050269)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hand-foot-and-mouth disease (10019113)	3	0.5	0.1	1.6	4	0.6	0.2	1.6	2	0.4	0.0	1.3	4	0.6	0.2	1.6
	Herpangina (10019936)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Impetigo (10021531)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Influenza (10022000)	6	1.1	0.4	2.4	1	0.2	0.0	0.8	4	0.7	0.2	1.8	3	0.5	0.1	1.3
	Lice infestation (10024424)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Localised infection (10024774)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Lower respiratory tract infection (10024968)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Molluscum contagiosum (10027807)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Nasopharyngitis (10028810)	46	8.4	6.2	11.0	20	3.0	1.9	4.7	37	6.6	4.7	9.0	17	2.6	1.5	4.1
	Neonatal candida infection (10028924)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Oral candidiasis (10030963)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Otitis externa (10033072)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Otitis media (10033078)	39	7.1	5.1	9.6	22	3.3	2.1	5.0	34	6.1	4.2	8.4	15	2.3	1.3	3.7
	Otitis media acute (10033079)	15	2.7	1.5	4.5	3	0.5	0.1	1.3	14	2.5	1.4	4.2	4	0.6	0.2	1.6
	Paronychia (10034016)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Periorbital cellulitis (10057182)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pharyngitis (10034835)	6	1.1	0.4	2.4	8	1.2	0.5	2.4	11	2.0	1.0	3.5	4	0.6	0.2	1.6
	Pharyngitis streptococcal (10034839)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Pharyngotonsillitis (10049140)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	5	0.9	0.3	2.1	0	0.0	0.0	0.6
	Pneumonia (10035664)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	3	0.5	0.1	1.6	3	0.5	0.1	1.3

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pneumonia mycoplasmal (10035724)	0	0.0	0.0	0.7	3	0.5	0.1	1.3	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pneumonia viral (10035737)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Purulent discharge (10037569)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rash pustular (10037888)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Respiratory syncytial virus infection (10061603)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	4	0.7	0.2	1.8	0	0.0	0.0	0.6
	Respiratory tract infection (10062352)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Respiratory tract infection viral (10062106)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rhinitis (10039083)	4	0.7	0.2	1.9	6	0.9	0.3	2.0	4	0.7	0.2	1.8	2	0.3	0.0	1.1
	Sinusitis (10040753)	3	0.5	0.1	1.6	3	0.5	0.1	1.3	7	1.3	0.5	2.6	4	0.6	0.2	1.6
	Skin candida (10054152)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Skin infection (10040872)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Staphylococcal infection (10058080)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Streptococcal infection (10061372)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Tinea capitis (10043866)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Tonsillitis (10044008)	3	0.5	0.1	1.6	1	0.2	0.0	0.8	4	0.7	0.2	1.8	2	0.3	0.0	1.1
	Tracheitis (10044302)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Upper respiratory tract infection (10046306)	72	13.1	10.4	16.2	39	5.9	4.3	8.0	74	13.2	10.5	16.3	28	4.3	2.9	6.1
	Urinary tract infection (10046571)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Varicella (10046980)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Viral infection (10047461)	5	0.9	0.3	2.1	4	0.6	0.2	1.6	7	1.3	0.5	2.6	8	1.2	0.5	2.4
	Viral rash (10047476)	10	1.8	0.9	3.3	1	0.2	0.0	0.8	2	0.4	0.0	1.3	3	0.5	0.1	1.3
	Viral upper respiratory tract infection (10047482)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	7	1.3	0.5	2.6	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Animal bite (10002515)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Arthropod bite (10003399)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Burns second degree (10006802)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Concussion (10010254)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Contusion (10050584)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Corneal abrasion (10010984)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Eyelid contusion (10075018)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Face injury (10050392)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Fall (10016173)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Foreign body (10070245)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hand fracture (10019114)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Head injury (10019196)	2	0.4	0.0	1.3	2	0.3	0.0	1.1	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Joint dislocation (10023204)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Laceration (10023572)	3	0.5	0.1	1.6	3	0.5	0.1	1.3	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Limb injury (10061225)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Mouth injury (10049294)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Procedural pain (10064882)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Radial head dislocation (10073749)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rib fracture (10039117)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Scratch (10039737)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Skin abrasion (10064990)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Tooth injury (10044043)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Upper limb fracture (10061394)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Wound (10052428)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Investigations (10022891)	Blood lead increased (10005642)	1	0.2	0.0	1.0	3	0.5	0.1	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Body temperature increased (10005911)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Heart rate increased (10019303)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	4	0.7	0.2	1.8	1	0.2	0.0	0.8

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Musculoskeletal and connective tissue disorders (10028395)	Blount's disease (10072255)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Myalgia (10028411)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Pain in extremity (10033425)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Melanocytic naevus (10027145)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Skin papilloma (10040907)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Nervous system disorders (10029205)	Balance disorder (10049848)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dizziness (10013573)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Febrile convulsion (10016284)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Headache (10019211)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	1	0.2	0.0	1.0	2	0.3	0.0	1.1
	Psychomotor hyperactivity (10037211)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Speech disorder developmental (10041467)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	4	0.7	0.2	1.8	2	0.3	0.0	1.1
	Irritability (10022998)	4	0.7	0.2	1.9	0	0.0	0.0	0.6	5	0.9	0.3	2.1	0	0.0	0.0	0.6
	Sleep disorder (10040984)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Renal and urinary disorders (10038359)	Urinary tract disorder (10046566)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Genital labial adhesions (10064162)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Genital rash (10018175)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	1	0.2	0.0	0.8
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Asthma (10003553)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Bronchial hyperreactivity (10066091)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Bronchospasm (10006482)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Cough (10011224)	34	6.2	4.3	8.5	36	5.5	3.9	7.5	41	7.3	5.3	9.8	36	5.5	3.9	7.5
	Dysphonia (10013952)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dyspnoea (10013968)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Epistaxis (10015090)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Nasal congestion (10028735)	15	2.7	1.5	4.5	10	1.5	0.7	2.8	10	1.8	0.9	3.3	9	1.4	0.6	2.6
	Nasal discharge discolouration (10071553)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Oropharyngeal pain (10068319)	2	0.4	0.0	1.3	5	0.8	0.2	1.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pulmonary congestion (10037368)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Respiratory disorder (10038683)	2	0.4	0.0	1.3	4	0.6	0.2	1.6	4	0.7	0.2	1.8	1	0.2	0.0	0.8
	Respiratory distress (10038687)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Respiratory tract congestion (10052251)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rhinitis allergic (10039085)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rhinorrhoea (10039101)	31	5.6	3.9	7.9	28	4.3	2.9	6.1	38	6.8	4.8	9.2	38	5.8	4.1	7.9
	Sinus congestion (10040742)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Sinus disorder (10062244)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Sneezing (10041232)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	5	0.9	0.3	2.1	5	0.8	0.2	1.8
	Wheezing (10047924)	3	0.5	0.1	1.6	2	0.3	0.0	1.1	5	0.9	0.3	2.1	3	0.5	0.1	1.3
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Blister (10005191)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Dermal cyst (10012426)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Dermatitis (10012431)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dermatitis acneiform (10012432)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Dermatitis atopic (10012438)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	5	0.9	0.3	2.1	0	0.0	0.0	0.6
	Dermatitis contact (10012442)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Dermatitis diaper (10012444)	20	3.6	2.2	5.6	4	0.6	0.2	1.6	9	1.6	0.7	3.0	4	0.6	0.2	1.6
	Dry skin (10013786)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Ecchymosis (10014080)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Eczema (10014184)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	5	0.9	0.3	2.1	1	0.2	0.0	0.8
	Erythema (10015150)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	4	0.6	0.2	1.6
	Hyperhidrosis (10020642)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Keratosis pilaris (10066295)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Night sweats (10029410)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Prurigo (10037083)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pruritus (10037087)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rash (10037844)	12	2.2	1.1	3.8	4	0.6	0.2	1.6	9	1.6	0.7	3.0	4	0.6	0.2	1.6
	Rash erythematous (10037855)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Rash generalised (10037858)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rash macular (10037867)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Rash papular (10037876)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rash pruritic (10037884)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Skin fissures (10040849)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Skin irritation (10040880)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Skin lesion (10040882)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Urticaria (10046735)	3	0.5	0.1	1.6	1	0.2	0.0	0.8	2	0.4	0.0	1.3	4	0.6	0.2	1.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 122 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		398	37.2	34.3	40.2	239	36.4	32.7	40.2	383	35.2	32.3	38.1	235	35.8	32.1	39.6
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Iron deficiency anaemia (10022972)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Leukocytosis (10024378)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Lymphadenopathy (10025197)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Neutropenia (10029354)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Congenital, familial and genetic disorders (10010331)	Phimosis (10034878)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Tibial torsion (10064515)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	0	0.0	0.0	0.3	2	0.3	0.0	1.1	3	0.3	0.1	0.8	2	0.3	0.0	1.1
	Ear discomfort (10052137)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Ear pain (10014020)	2	0.2	0.0	0.7	4	0.6	0.2	1.6	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Middle ear effusion (10062545)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Dacryostenosis acquired (10053990)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Eye discharge (10015915)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Eye pruritus (10052140)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Eyelid oedema (10015993)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Lacrimation increased (10023644)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Photophobia (10034960)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Gastrointestinal disorders (10017947)	Abdominal discomfort (10000059)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Abdominal hernia (10060954)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Abdominal pain upper (10000087)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Constipation (10010774)	4	0.4	0.1	1.0	1	0.2	0.0	0.8	4	0.4	0.1	0.9	1	0.2	0.0	0.8
	Dental caries (10012318)	0	0.0	0.0	0.3	3	0.5	0.1	1.3	0	0.0	0.0	0.3	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Diarrhoea (10012735)	45	4.2	3.1	5.6	27	4.1	2.7	5.9	21	1.9	1.2	2.9	32	4.9	3.4	6.8
	Faeces hard (10016101)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Flatulence (10016766)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Food poisoning (10016952)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Frequent bowel movements (10017367)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Gastrooesophageal reflux disease (10017885)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Haematochezia (10018836)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Intussusception (10022863)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Nausea (10028813)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Regurgitation (10067171)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Stomatitis (10042128)	0	0.0	0.0	0.3	2	0.3	0.0	1.1	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Teething (10043183)	16	1.5	0.9	2.4	2	0.3	0.0	1.1	17	1.6	0.9	2.5	5	0.8	0.2	1.8
	Vomiting (10047700)	31	2.9	2.0	4.1	17	2.6	1.5	4.1	22	2.0	1.3	3.0	25	3.8	2.5	5.6
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Administration site rash (10071156)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Asthenia (10003549)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Chills (10008531)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Developmental delay (10012559)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Discomfort (10013082)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Fatigue (10016256)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Feeling hot (10016334)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Ill-defined disorder (10061520)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Influenza like illness (10022004)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Injection site bruising (10022052)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Injection site pruritus (10022093)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Injection site rash (10022094)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Injection site warmth (10022112)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Local swelling (10024770)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Malaise (10025482)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Pain (10033371)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Pyrexia (10037660)	26	2.4	1.6	3.5	28	4.3	2.9	6.1	38	3.5	2.5	4.8	20	3.0	1.9	4.7
	Thirst (10043458)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Vaccination site pain (10068879)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Vaccination site rash (10069482)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Vaccination site reaction (10059080)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Vaccination site swelling (10069620)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Vessel puncture site haemorrhage (10054092)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Immune system disorders (10021428)	Drug hypersensitivity (10013700)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Hypersensitivity (10020751)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Multiple allergies (10028164)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Seasonal allergy (10048908)	0	0.0	0.0	0.3	2	0.3	0.0	1.1	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Acarodermatitis (10063409)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Acute sinusitis (10001076)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	3	0.3	0.1	0.8	2	0.3	0.0	1.1
	Bronchiolitis (10006448)	9	0.8	0.4	1.6	0	0.0	0.0	0.6	15	1.4	0.8	2.3	1	0.2	0.0	0.8
	Bronchitis (10006451)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	7	0.6	0.3	1.3	2	0.3	0.0	1.1
	Candida infection (10074170)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	3	0.3	0.1	0.8	0	0.0	0.0	0.6
	Candida nappy rash (10007135)	4	0.4	0.1	1.0	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Cellulitis (10007882)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Clostridium difficile infection (10054236)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Conjunctivitis (10010741)	9	0.8	0.4	1.6	4	0.6	0.2	1.6	13	1.2	0.6	2.0	7	1.1	0.4	2.2
	Conjunctivitis bacterial (10061784)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Coxsackie viral infection (10011261)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Croup infectious (10011416)	7	0.7	0.3	1.3	8	1.2	0.5	2.4	9	0.8	0.4	1.6	5	0.8	0.2	1.8
	Dermatophytosis (10012504)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Ear infection (10014011)	7	0.7	0.3	1.3	3	0.5	0.1	1.3	9	0.8	0.4	1.6	2	0.3	0.0	1.1
	Enterobiasis (10014881)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Exanthema subitum (10015586)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Eye infection (10015929)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Folliculitis (10016936)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Fungal infection (10017533)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Fungal skin infection (10017543)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Gastroenteritis (10017888)	8	0.7	0.3	1.5	7	1.1	0.4	2.2	17	1.6	0.9	2.5	5	0.8	0.2	1.8
	Gastroenteritis viral (10017918)	3	0.3	0.1	0.8	1	0.2	0.0	0.8	3	0.3	0.1	0.8	1	0.2	0.0	0.8
	Genital candidiasis (10018143)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Groin abscess (10050269)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Hand-foot-and-mouth disease (10019113)	3	0.3	0.1	0.8	4	0.6	0.2	1.6	2	0.2	0.0	0.7	4	0.6	0.2	1.6
	Herpangina (10019936)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Impetigo (10021531)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Influenza (10022000)	6	0.6	0.2	1.2	1	0.2	0.0	0.8	4	0.4	0.1	0.9	3	0.5	0.1	1.3
	Lice infestation (10024424)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Localised infection (10024774)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Lower respiratory tract infection (10024968)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Molluscum contagiosum (10027807)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Nasopharyngitis (10028810)	48	4.5	3.3	5.9	20	3.0	1.9	4.7	44	4.0	3.0	5.4	17	2.6	1.5	4.1
	Neonatal candida infection (10028924)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Oral candidiasis (10030963)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Otitis externa (10033072)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Otitis media (10033078)	40	3.7	2.7	5.1	22	3.3	2.1	5.0	36	3.3	2.3	4.5	15	2.3	1.3	3.7
	Otitis media acute (10033079)	15	1.4	0.8	2.3	3	0.5	0.1	1.3	14	1.3	0.7	2.1	4	0.6	0.2	1.6
	Paronychia (10034016)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Periorbital cellulitis (10057182)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Pharyngitis (10034835)	6	0.6	0.2	1.2	8	1.2	0.5	2.4	11	1.0	0.5	1.8	4	0.6	0.2	1.6
	Pharyngitis streptococcal (10034839)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	3	0.3	0.1	0.8	1	0.2	0.0	0.8
	Pharyngotonsillitis (10049140)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	5	0.5	0.1	1.1	0	0.0	0.0	0.6
	Pneumonia (10035664)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	3	0.3	0.1	0.8	3	0.5	0.1	1.3
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Pneumonia mycoplasmal (10035724)	0	0.0	0.0	0.3	3	0.5	0.1	1.3	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Pneumonia viral (10035737)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Purulent discharge (10037569)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rash pustular (10037888)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Respiratory syncytial virus bronchiolitis (10038718)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Respiratory syncytial virus infection (10061603)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	4	0.4	0.1	0.9	0	0.0	0.0	0.6
	Respiratory tract infection (10062352)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Respiratory tract infection viral (10062106)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Rhinitis (10039083)	4	0.4	0.1	1.0	6	0.9	0.3	2.0	4	0.4	0.1	0.9	2	0.3	0.0	1.1
	Sinusitis (10040753)	3	0.3	0.1	0.8	3	0.5	0.1	1.3	8	0.7	0.3	1.4	4	0.6	0.2	1.6
	Skin candida (10054152)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Skin infection (10040872)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Staphylococcal infection (10058080)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Streptococcal infection (10061372)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Tinea capitis (10043866)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Tonsillitis (10044008)	3	0.3	0.1	0.8	1	0.2	0.0	0.8	4	0.4	0.1	0.9	2	0.3	0.0	1.1
	Tracheitis (10044302)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Upper respiratory tract infection (10046306)	75	7.0	5.6	8.7	39	5.9	4.3	8.0	80	7.3	5.9	9.1	28	4.3	2.9	6.1
	Urinary tract infection (10046571)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Varicella (10046980)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Viral infection (10047461)	5	0.5	0.2	1.1	4	0.6	0.2	1.6	7	0.6	0.3	1.3	8	1.2	0.5	2.4
	Viral rash (10047476)	10	0.9	0.4	1.7	1	0.2	0.0	0.8	2	0.2	0.0	0.7	3	0.5	0.1	1.3
	Viral upper respiratory tract infection (10047482)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	7	0.6	0.3	1.3	0	0.0	0.0	0.6

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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Animal bite (10002515)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Arthropod bite (10003399)	0	0.0	0.0	0.3	2	0.3	0.0	1.1	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Burns second degree (10006802)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Concussion (10010254)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Contusion (10050584)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Corneal abrasion (10010984)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Eyelid contusion (10075018)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Face injury (10050392)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Fall (10016173)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Foreign body (10070245)	0	0.0	0.0	0.3	2	0.3	0.0	1.1	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Hand fracture (10019114)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Head injury (10019196)	2	0.2	0.0	0.7	2	0.3	0.0	1.1	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Joint dislocation (10023204)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Laceration (10023572)	3	0.3	0.1	0.8	3	0.5	0.1	1.3	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Limb injury (10061225)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Mouth injury (10049294)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Procedural pain (10064882)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Radial head dislocation (10073749)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rib fracture (10039117)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Scratch (10039737)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Skin abrasion (10064990)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Tooth injury (10044043)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Upper limb fracture (10061394)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Wound (10052428)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Investigations (10022891)	Blood lead increased (10005642)	1	0.1	0.0	0.5	3	0.5	0.1	1.3	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Body temperature increased (10005911)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Heart rate increased (10019303)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	4	0.4	0.1	0.9	1	0.2	0.0	0.8

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Musculoskeletal and connective tissue disorders (10028395)	Blount's disease (10072255)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Myalgia (10028411)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Pain in extremity (10033425)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	Melanocytic naevus (10027145)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Skin papilloma (10040907)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Nervous system disorders (10029205)	Balance disorder (10049848)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Dizziness (10013573)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Febrile convulsion (10016284)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Headache (10019211)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	1	0.1	0.0	0.5	2	0.3	0.0	1.1
	Psychomotor hyperactivity (10037211)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Speech disorder developmental (10041467)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	4	0.4	0.1	0.9	2	0.3	0.0	1.1
	Irritability (10022998)	4	0.4	0.1	1.0	0	0.0	0.0	0.6	5	0.5	0.1	1.1	0	0.0	0.0	0.6
	Sleep disorder (10040984)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Renal and urinary disorders (10038359)	Urinary tract disorder (10046566)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Genital labial adhesions (10064162)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Genital rash (10018175)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	1	0.2	0.0	0.8
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Asthma (10003553)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Bronchial hyperreactivity (10066091)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Bronchospasm (10006482)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Cough (10011224)	36	3.4	2.4	4.6	36	5.5	3.9	7.5	42	3.9	2.8	5.2	36	5.5	3.9	7.5
	Dysphonia (10013952)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Dyspnoea (10013968)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Epistaxis (10015090)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Nasal congestion (10028735)	15	1.4	0.8	2.3	10	1.5	0.7	2.8	10	0.9	0.4	1.7	9	1.4	0.6	2.6
	Nasal discharge discolouration (10071553)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Oropharyngeal pain (10068319)	2	0.2	0.0	0.7	5	0.8	0.2	1.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Pulmonary congestion (10037368)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Respiratory disorder (10038683)	2	0.2	0.0	0.7	4	0.6	0.2	1.6	4	0.4	0.1	0.9	1	0.2	0.0	0.8
	Respiratory distress (10038687)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Respiratory tract congestion (10052251)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rhinitis allergic (10039085)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rhinorrhoea (10039101)	32	3.0	2.1	4.2	28	4.3	2.9	6.1	40	3.7	2.6	5.0	38	5.8	4.1	7.9
	Sinus congestion (10040742)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Sinus disorder (10062244)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Sneezing (10041232)	2	0.2	0.0	0.7	1	0.2	0.0	0.8	5	0.5	0.1	1.1	5	0.8	0.2	1.8
	Wheezing (10047924)	3	0.3	0.1	0.8	2	0.3	0.0	1.1	5	0.5	0.1	1.1	3	0.5	0.1	1.3
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Blister (10005191)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Dermal cyst (10012426)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Dermatitis (10012431)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Dermatitis acneiform (10012432)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Dermatitis atopic (10012438)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	5	0.5	0.1	1.1	0	0.0	0.0	0.6
	Dermatitis contact (10012442)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	3	0.3	0.1	0.8	1	0.2	0.0	0.8
	Dermatitis diaper (10012444)	22	2.1	1.3	3.1	4	0.6	0.2	1.6	9	0.8	0.4	1.6	4	0.6	0.2	1.6
	Dry skin (10013786)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Ecchymosis (10014080)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Eczema (10014184)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	5	0.5	0.1	1.1	1	0.2	0.0	0.8
	Erythema (10015150)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	4	0.6	0.2	1.6
	Hyperhidrosis (10020642)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Keratosis pilaris (10066295)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Night sweats (10029410)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Prurigo (10037083)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Pruritus (10037087)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rash (10037844)	12	1.1	0.6	2.0	4	0.6	0.2	1.6	10	0.9	0.4	1.7	4	0.6	0.2	1.6
	Rash erythematous (10037855)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Rash generalised (10037858)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rash macular (10037867)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Rash papular (10037876)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rash pruritic (10037884)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Skin fissures (10040849)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Skin irritation (10040880)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Skin lesion (10040882)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Urticaria (10046735)	3	0.3	0.1	0.8	1	0.2	0.0	0.8	2	0.2	0.0	0.7	4	0.6	0.2	1.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 123 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		35	6.4	4.5	8.7	35	5.3	3.7	7.3	48	8.6	6.4	11.2	27	4.1	2.7	5.9
Ear and labyrinth disorders (10013993)	Middle ear effusion (10062545)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Eye discharge (10015915)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Diarrhoea (10012735)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	2	0.4	0.0	1.3	4	0.6	0.2	1.6
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Nausea (10028813)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Stomatitis (10042128)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Vomiting (10047700)	4	0.7	0.2	1.9	5	0.8	0.2	1.8	7	1.3	0.5	2.6	6	0.9	0.3	2.0
General disorders and administration site conditions (10018065)	Chills (10008531)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Injection site pruritus (10022093)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pain (10033371)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pyrexia (10037660)	3	0.5	0.1	1.6	9	1.4	0.6	2.6	10	1.8	0.9	3.3	3	0.5	0.1	1.3
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Bronchiolitis (10006448)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	4	0.7	0.2	1.8	1	0.2	0.0	0.8
	Candida infection (10074170)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Cellulitis (10007882)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Conjunctivitis (10010741)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Croup infectious (10011416)	2	0.4	0.0	1.3	3	0.5	0.1	1.3	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Ear infection (10014011)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Gastroenteritis (10017888)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Gastroenteritis viral (10017918)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Groin abscess (10050269)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hand-foot-and-mouth disease (10019113)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Herpangina (10019936)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Influenza (10022000)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Nasopharyngitis (10028810)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	5	0.9	0.3	2.1	0	0.0	0.0	0.6
	Otitis media (10033078)	6	1.1	0.4	2.4	4	0.6	0.2	1.6	3	0.5	0.1	1.6	3	0.5	0.1	1.3
	Otitis media acute (10033079)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Pharyngitis (10034835)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pneumonia (10035664)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Pneumonia mycoplasmal (10035724)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rhinitis (10039083)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Sinusitis (10040753)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Staphylococcal infection (10058080)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tonsillitis (10044008)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Upper respiratory tract infection (10046306)	6	1.1	0.4	2.4	4	0.6	0.2	1.6	5	0.9	0.3	2.1	2	0.3	0.0	1.1
	Viral infection (10047461)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
Injury, poisoning and procedural complications (10022117)	Face injury (10050392)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hand fracture (10019114)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Laceration (10023572)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Mouth injury (10049294)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Radial head dislocation (10073749)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Investigations (10022891)	Heart rate increased (10019303)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Headache (10019211)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Cough (10011224)	3	0.5	0.1	1.6	1	0.2	0.0	0.8	3	0.5	0.1	1.6	3	0.5	0.1	1.3
	Dyspnoea (10013968)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Nasal congestion (10028735)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Oropharyngeal pain (10068319)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Respiratory disorder (10038683)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Rhinorrhoea (10039101)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	3	0.5	0.1	1.3
	Wheezing (10047924)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dermatitis diaper (10012444)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rash (10037844)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Urticaria (10046735)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 124 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		37	3.5	2.4	4.7	35	5.3	3.7	7.3	52	4.8	3.6	6.2	27	4.1	2.7	5.9
Ear and labyrinth disorders (10013993)	Middle ear effusion (10062545)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Eye disorders (10015919)	Chalazion (10008388)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Eye discharge (10015915)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Constipation (10010774)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Diarrhoea (10012735)	1	0.1	0.0	0.5	2	0.3	0.0	1.1	2	0.2	0.0	0.7	4	0.6	0.2	1.6
	Intussusception (10022863)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Nausea (10028813)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Stomatitis (10042128)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Vomiting (10047700)	4	0.4	0.1	1.0	5	0.8	0.2	1.8	7	0.6	0.3	1.3	6	0.9	0.3	2.0
General disorders and administration site conditions (10018065)	Chills (10008531)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Injection site pruritus (10022093)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Pain (10033371)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Pyrexia (10037660)	3	0.3	0.1	0.8	9	1.4	0.6	2.6	11	1.0	0.5	1.8	3	0.5	0.1	1.3
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Bronchiolitis (10006448)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	4	0.4	0.1	0.9	1	0.2	0.0	0.8
	Candida infection (10074170)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Cellulitis (10007882)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Conjunctivitis (10010741)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Croup infectious (10011416)	2	0.2	0.0	0.7	3	0.5	0.1	1.3	3	0.3	0.1	0.8	1	0.2	0.0	0.8
	Ear infection (10014011)	1	0.1	0.0	0.5	2	0.3	0.0	1.1	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Gastroenteritis (10017888)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Gastroenteritis viral (10017918)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Groin abscess (10050269)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Hand-foot-and-mouth disease (10019113)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Herpangina (10019936)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Influenza (10022000)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Nasopharyngitis (10028810)	1	0.1	0.0	0.5	2	0.3	0.0	1.1	5	0.5	0.1	1.1	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Otitis media (10033078)	6	0.6	0.2	1.2	4	0.6	0.2	1.6	3	0.3	0.1	0.8	3	0.5	0.1	1.3
	Otitis media acute (10033079)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Pharyngitis (10034835)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Pharyngitis streptococcal (10034839)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Pneumonia (10035664)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Pneumonia mycoplasmal (10035724)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rhinitis (10039083)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Sinusitis (10040753)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Staphylococcal abscess (10041917)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Staphylococcal infection (10058080)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Tonsillitis (10044008)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Upper respiratory tract infection (10046306)	6	0.6	0.2	1.2	4	0.6	0.2	1.6	5	0.5	0.1	1.1	2	0.3	0.0	1.1
	Viral infection (10047461)	0	0.0	0.0	0.3	2	0.3	0.0	1.1	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Viral upper respiratory tract infection (10047482)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
Injury, poisoning and procedural complications (10022117)	Face injury (10050392)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Hand fracture (10019114)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Laceration (10023572)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Mouth injury (10049294)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Radial head dislocation (10073749)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Investigations (10022891)	Heart rate increased (10019303)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Metabolism and nutrition disorders (10027433)	Decreased appetite (10061428)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Headache (10019211)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Bronchial hyperreactivity (10066091)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Cough (10011224)	3	0.3	0.1	0.8	1	0.2	0.0	0.8	3	0.3	0.1	0.8	3	0.5	0.1	1.3
	Dyspnoea (10013968)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Nasal congestion (10028735)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Oropharyngeal pain (10068319)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Respiratory disorder (10038683)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Rhinorrhoea (10039101)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	3	0.5	0.1	1.3
	Wheezing (10047924)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Dermatitis diaper (10012444)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Rash (10037844)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Urticaria (10046735)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	1	0.2	0.0	0.8

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 125 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		40	7.3	5.2	9.8	31	4.7	3.2	6.6	35	6.3	4.4	8.6	36	5.5	3.9	7.5
Blood and lymphatic system disorders (10005329)	Lymphadenopathy (10025197)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Ear and labyrinth disorders (10013993)	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Eye disorders (10015919)	Eye discharge (10015915)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Lacrimation increased (10023644)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Diarrhoea (10012735)	6	1.1	0.4	2.4	6	0.9	0.3	2.0	3	0.5	0.1	1.6	10	1.5	0.7	2.8
	Vomiting (10047700)	9	1.6	0.8	3.1	4	0.6	0.2	1.6	4	0.7	0.2	1.8	9	1.4	0.6	2.6
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Administration site rash (10071156)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Chills (10008531)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Feeling hot (10016334)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Injection site bruising (10022052)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Injection site rash (10022094)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Injection site warmth (10022112)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Local swelling (10024770)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Malaise (10025482)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pain (10033371)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pyrexia (10037660)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	4	0.7	0.2	1.8	0	0.0	0.0	0.6
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Immune system disorders (10021428)	Multiple allergies (10028164)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Infections and infestations (10021881)	Conjunctivitis (10010741)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Croup infectious (10011416)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Influenza (10022000)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Nasopharyngitis (10028810)	2	0.4	0.0	1.3	3	0.5	0.1	1.3	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Otitis media (10033078)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Pharyngitis (10034835)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rhinitis (10039083)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Upper respiratory tract infection (10046306)	6	1.1	0.4	2.4	3	0.5	0.1	1.3	4	0.7	0.2	1.8	0	0.0	0.0	0.6
	Viral infection (10047461)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Nervous system disorders (10029205)	Headache (10019211)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	2	0.4	0.0	1.3	4	0.6	0.2	1.6	7	1.3	0.5	2.6	5	0.8	0.2	1.8
	Nasal congestion (10028735)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	4	0.7	0.2	1.8	3	0.5	0.1	1.3
	Rhinorrhoea (10039101)	7	1.3	0.5	2.6	2	0.3	0.0	1.1	9	1.6	0.7	3.0	6	0.9	0.3	2.0
	Sneezing (10041232)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Wheezing (10047924)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Skin and subcutaneous tissue disorders (10040785)	Dermatitis acneiform (10012432)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Dermatitis diaper (10012444)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Erythema (10015150)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Hyperhidrosis (10020642)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Rash (10037844)	3	0.5	0.1	1.6	3	0.5	0.1	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rash generalised (10037858)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rash papular (10037876)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Skin fissures (10040849)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Urticaria (10046735)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	3	0.5	0.1	1.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 126 Percentage of doses with unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		44	4.1	3.0	5.5	31	4.7	3.2	6.6	37	3.4	2.4	4.7	36	5.5	3.9	7.5
Blood and lymphatic system disorders (10005329)	Lymphadenopathy (10025197)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Ear and labyrinth disorders (10013993)	Eustachian tube dysfunction (10015543)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Lacrimation increased (10023644)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Diarrhoea (10012735)	7	0.7	0.3	1.3	6	0.9	0.3	2.0	3	0.3	0.1	0.8	10	1.5	0.7	2.8
	Vomiting (10047700)	9	0.8	0.4	1.6	4	0.6	0.2	1.6	4	0.4	0.1	0.9	9	1.4	0.6	2.6
General disorders and administration site conditions (10018065)	Administration site bruise (10075094)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Administration site rash (10071156)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Chills (10008531)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Feeling hot (10016334)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Injection site bruising (10022052)	2	0.2	0.0	0.7	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Injection site rash (10022094)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Injection site warmth (10022112)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Local swelling (10024770)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Malaise (10025482)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Pain (10033371)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Pyrexia (10037660)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	4	0.4	0.1	0.9	0	0.0	0.0	0.6
	Vaccination site pruritus (10068881)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Immune system disorders (10021428)	Multiple allergies (10028164)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Infections and infestations (10021881)	Conjunctivitis (10010741)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Croup infectious (10011416)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Influenza (10022000)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Nasopharyngitis (10028810)	2	0.2	0.0	0.7	3	0.5	0.1	1.3	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Otitis media (10033078)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	2	0.2	0.0	0.7	0	0.0	0.0	0.6
	Pharyngitis (10034835)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rhinitis (10039083)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Upper respiratory tract infection (10046306)	6	0.6	0.2	1.2	3	0.5	0.1	1.3	4	0.4	0.1	0.9	0	0.0	0.0	0.6
	Viral infection (10047461)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Nervous system disorders (10029205)	Headache (10019211)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Somnolence (10041349)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	1	0.2	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	2	0.2	0.0	0.7	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	2	0.2	0.0	0.7	4	0.6	0.2	1.6	7	0.6	0.3	1.3	5	0.8	0.2	1.8
	Nasal congestion (10028735)	1	0.1	0.0	0.5	2	0.3	0.0	1.1	4	0.4	0.1	0.9	3	0.5	0.1	1.3
	Rhinorrhoea (10039101)	7	0.7	0.3	1.3	2	0.3	0.0	1.1	10	0.9	0.4	1.7	6	0.9	0.3	2.0
	Sneezing (10041232)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	2	0.2	0.0	0.7	1	0.2	0.0	0.8
	Wheezing (10047924)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
Skin and subcutaneous tissue disorders (10040785)	Dermatitis acneiform (10012432)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Dermatitis diaper (10012444)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Erythema (10015150)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	2	0.3	0.0	1.1
	Hyperhidrosis (10020642)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Rash (10037844)	3	0.3	0.1	0.8	3	0.5	0.1	1.3	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rash generalised (10037858)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Rash papular (10037876)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Skin fissures (10040849)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Urticaria (10046735)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	3	0.5	0.1	1.3

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom

Table 127 Percentage of subjects reporting the occurrence of grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		4	0.7	0.2	1.9	3	0.5	0.1	1.3	5	0.9	0.3	2.1	4	0.6	0.2	1.6
Eye disorders (10015919)	Eye discharge (10015915)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Vomiting (10047700)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	1	0.2	0.0	1.0	2	0.3	0.0	1.1
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Nasopharyngitis (10028810)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Otitis media (10033078)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Upper respiratory tract infection (10046306)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Viral infection (10047461)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Nervous system disorders (10029205)	Somnolence (10041349)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rhinorrhoea (10039101)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Wheezing (10047924)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 128 Percentage of doses with grade 3 unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with causal relationship to vaccination, within the 28-day (Days 0-27) post-vaccination period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 1069				PRIM N = 657				UNPRIM N = 1089				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		4	0.4	0.1	1.0	3	0.5	0.1	1.3	5	0.5	0.1	1.1	4	0.6	0.2	1.6
Eye disorders (10015919)	Eye discharge (10015915)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Vomiting (10047700)	1	0.1	0.0	0.5	1	0.2	0.0	0.8	1	0.1	0.0	0.5	2	0.3	0.0	1.1
General disorders and administration site conditions (10018065)	Pyrexia (10037660)	0	0.0	0.0	0.3	1	0.2	0.0	0.8	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Infections and infestations (10021881)	Croup infectious (10011416)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Nasopharyngitis (10028810)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Otitis media (10033078)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Upper respiratory tract infection (10046306)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6
	Viral infection (10047461)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Nervous system disorders (10029205)	Somnolence (10041349)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Psychiatric disorders (10037175)	Insomnia (10022437)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Irritability (10022998)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	1	0.1	0.0	0.5	0	0.0	0.0	0.6
	Rhinorrhoea (10039101)	0	0.0	0.0	0.3	0	0.0	0.0	0.6	0	0.0	0.0	0.3	1	0.2	0.0	0.8
	Wheezing (10047924)	1	0.1	0.0	0.5	0	0.0	0.0	0.6	0	0.0	0.0	0.3	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 129 Percentage of subjects reporting the occurrence of unsolicited AEs classified by MedDRA Primary System Organ Class and Preferred Term with medically attended visit (MAEs) during the entire study period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		344	62.5	58.4	66.6	383	58.3	54.4	62.1	337	60.2	56.0	64.3	382	58.1	54.3	61.9
Blood and lymphatic system disorders (10005329)	Anaemia (10002034)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	3	0.5	0.1	1.6	4	0.6	0.2	1.6
	Iron deficiency anaemia (10022972)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	2	0.3	0.0	1.1
	Leukocytosis (10024378)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	3	0.5	0.1	1.6	2	0.3	0.0	1.1
	Lymphadenitis (10025188)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Lymphadenopathy (10025197)	2	0.4	0.0	1.3	4	0.6	0.2	1.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Neutropenia (10029354)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Congenital, familial and genetic disorders (10010331)	Cryptorchism (10011498)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Cytogenetic abnormality (10067477)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Dermoid cyst (10012522)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Macrocephaly (10050183)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Phimosis (10034878)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Tibial torsion (10064515)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Ear and labyrinth disorders (10013993)	Cerumen impaction (10050337)	3	0.5	0.1	1.6	7	1.1	0.4	2.2	5	0.9	0.3	2.1	6	0.9	0.3	2.0
	Deafness bilateral (10052556)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Deafness unilateral (10048812)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Ear discomfort (10052137)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Ear disorder (10014004)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Ear pain (10014020)	4	0.7	0.2	1.9	9	1.4	0.6	2.6	5	0.9	0.3	2.1	9	1.4	0.6	2.6
	Eustachian tube dysfunction (10015543)	3	0.5	0.1	1.6	3	0.5	0.1	1.3	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Eustachian tube obstruction (10015544)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Middle ear effusion (10062545)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Otorrhoea (10033101)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Tympanic membrane hyperaemia (10052154)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tympanic membrane perforation (10045210)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Eye disorders (10015919)	Astigmatism (10003569)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Blepharitis (10005148)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Chalazion (10008388)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Conjunctival haemorrhage (10010719)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Conjunctivitis allergic (10010744)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Dacryostenosis acquired (10053990)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Eye discharge (10015915)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Eyelid oedema (10015993)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Photophobia (10034960)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Strabismus (10042159)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Gastrointestinal disorders (10017947)	Abdominal hernia (10060954)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Abdominal pain (10000081)	0	0.0	0.0	0.7	4	0.6	0.2	1.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Abdominal pain upper (10000087)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Anal fissure (10002153)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Anal polyp (10002168)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Anal pruritus (10068172)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Anal skin tags (10002172)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Aphthous stomatitis (10002958)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Constipation (10010774)	3	0.5	0.1	1.6	4	0.6	0.2	1.6	6	1.1	0.4	2.3	4	0.6	0.2	1.6
	Dental caries (10012318)	0	0.0	0.0	0.7	4	0.6	0.2	1.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Diarrhoea (10012735)	25	4.5	3.0	6.6	14	2.1	1.2	3.5	25	4.5	2.9	6.5	15	2.3	1.3	3.7
	Epigastric discomfort (10053155)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Eructation (10015137)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Flatulence (10016766)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Food poisoning (10016952)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Gastrointestinal inflammation (10064147)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Gastrooesophageal reflux disease (10017885)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Haematochezia (10018836)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Nausea (10028813)	4	0.7	0.2	1.9	2	0.3	0.0	1.1	1	0.2	0.0	1.0	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Oral disorder (10067621)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Post-tussive vomiting (10066220)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Stomatitis (10042128)	2	0.4	0.0	1.3	3	0.5	0.1	1.3	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Teething (10043183)	5	0.9	0.3	2.1	2	0.3	0.0	1.1	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Vomiting (10047700)	27	4.9	3.3	7.1	17	2.6	1.5	4.1	22	3.9	2.5	5.9	14	2.1	1.2	3.5
General disorders and administration site conditions (10018065)	Asthenia (10003549)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Crying (10011469)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Developmental delay (10012559)	1	0.2	0.0	1.0	3	0.5	0.1	1.3	2	0.4	0.0	1.3	3	0.5	0.1	1.3
	Fatigue (10016256)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Gait disturbance (10017577)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Influenza like illness (10022004)	0	0.0	0.0	0.7	3	0.5	0.1	1.3	0	0.0	0.0	0.7	3	0.5	0.1	1.3
	Local swelling (10024770)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pyrexia (10037660)	34	6.2	4.3	8.5	41	6.2	4.5	8.4	38	6.8	4.8	9.2	34	5.2	3.6	7.2
	Vaccination site rash (10069482)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Vaccination site reaction (10059080)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Vessel puncture site haemorrhage (10054092)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Immune system disorders (10021428)	Allergy to animal (10001742)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Drug hypersensitivity (10013700)	4	0.7	0.2	1.9	1	0.2	0.0	0.8	0	0.0	0.0	0.7	5	0.8	0.2	1.8
	Food allergy (10016946)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hypersensitivity (10020751)	1	0.2	0.0	1.0	3	0.5	0.1	1.3	2	0.4	0.0	1.3	2	0.3	0.0	1.1
	Immunodeficiency (10061598)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Multiple allergies (10028164)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Seasonal allergy (10048908)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Selective iga immunodeficiency (10039915)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Infections and infestations (10021881)	Abscess (10000269)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Abscess limb (10050473)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Acarodermatitis (10063409)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	3	0.5	0.1	1.3
	Acute sinusitis (10001076)	2	0.4	0.0	1.3	8	1.2	0.5	2.4	6	1.1	0.4	2.3	8	1.2	0.5	2.4
	Acute tonsillitis (10001093)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Adenoiditis (10051223)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Atypical mycobacterial infection (10061663)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Body tinea (10005913)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	1	0.2	0.0	1.0	2	0.3	0.0	1.1
	Bronchiolitis (10006448)	27	4.9	3.3	7.1	10	1.5	0.7	2.8	26	4.6	3.1	6.7	10	1.5	0.7	2.8
	Bronchitis (10006451)	4	0.7	0.2	1.9	6	0.9	0.3	2.0	10	1.8	0.9	3.3	15	2.3	1.3	3.7
	Candida infection (10074170)	3	0.5	0.1	1.6	1	0.2	0.0	0.8	7	1.3	0.5	2.6	0	0.0	0.0	0.6
	Candida nappy rash (10007135)	8	1.5	0.6	2.8	2	0.3	0.0	1.1	3	0.5	0.1	1.6	2	0.3	0.0	1.1
	Cellulitis (10007882)	3	0.5	0.1	1.6	3	0.5	0.1	1.3	3	0.5	0.1	1.6	5	0.8	0.2	1.8
	Clostridium difficile infection (10054236)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Conjunctivitis (10010741)	25	4.5	3.0	6.6	31	4.7	3.2	6.6	33	5.9	4.1	8.2	32	4.9	3.4	6.8
	Conjunctivitis bacterial (10061784)	3	0.5	0.1	1.6	2	0.3	0.0	1.1	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Conjunctivitis viral (10010755)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Coxsackie viral infection (10011261)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Croup infectious (10011416)	21	3.8	2.4	5.8	37	5.6	4.0	7.7	21	3.8	2.3	5.7	26	4.0	2.6	5.7
	Dacryocystitis (10011844)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Dermatophytosis (10012504)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Ear infection (10014011)	11	2.0	1.0	3.6	5	0.8	0.2	1.8	10	1.8	0.9	3.3	7	1.1	0.4	2.2
	Enterobiasis (10014881)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Exanthema subitum (10015586)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	External ear cellulitis (10015729)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Eye infection (10015929)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Folliculitis (10016936)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	4	0.6	0.2	1.6
	Fungal infection (10017533)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	2	0.3	0.0	1.1
	Fungal skin infection (10017543)	4	0.7	0.2	1.9	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Furuncle (10017553)	0	0.0	0.0	0.7	3	0.5	0.1	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Gastroenteritis (10017888)	29	5.3	3.6	7.5	30	4.6	3.1	6.5	35	6.3	4.4	8.6	32	4.9	3.4	6.8
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Gastroenteritis viral (10017918)	7	1.3	0.5	2.6	12	1.8	0.9	3.2	5	0.9	0.3	2.1	0	0.0	0.0	0.6
	Genital candidiasis (10018143)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Groin abscess (10050269)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hand-foot-and-mouth disease (10019113)	3	0.5	0.1	1.6	7	1.1	0.4	2.2	6	1.1	0.4	2.3	7	1.1	0.4	2.2

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Herpangina (10019936)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	2	0.4	0.0	1.3	2	0.3	0.0	1.1
	Hordeolum (10020377)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Impetigo (10021531)	2	0.4	0.0	1.3	5	0.8	0.2	1.8	2	0.4	0.0	1.3	5	0.8	0.2	1.8
	Infected bites (10021769)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Influenza (10022000)	11	2.0	1.0	3.6	12	1.8	0.9	3.2	14	2.5	1.4	4.2	14	2.1	1.2	3.5
	Laryngitis (10023874)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Lice infestation (10024424)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Localised infection (10024774)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Lower respiratory tract infection (10024968)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Molluscum contagiosum (10027807)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	3	0.5	0.1	1.3
	Myringitis bullous (10028659)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Nasopharyngitis (10028810)	40	7.3	5.2	9.8	11	1.7	0.8	3.0	32	5.7	3.9	8.0	14	2.1	1.2	3.5
	Neonatal candida infection (10028924)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Onychomycosis (10030338)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Oral candidiasis (10030963)	3	0.5	0.1	1.6	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Oropharyngeal candidiasis (10050346)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Otitis externa (10033072)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Otitis media (10033078)	100	18.2	15.0	21.7	94	14.3	11.7	17.2	117	20.9	17.6	24.5	105	16.0	13.3	19.0
	Otitis media acute (10033079)	34	6.2	4.3	8.5	31	4.7	3.2	6.6	40	7.1	5.2	9.6	28	4.3	2.9	6.1
	Otitis media chronic (10033081)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	1	0.2	0.0	1.0	5	0.8	0.2	1.8
	Paronychia (10034016)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Penile infection (10061912)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Periorbital cellulitis (10057182)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Pharyngitis (10034835)	19	3.5	2.1	5.3	25	3.8	2.5	5.6	27	4.8	3.2	6.9	20	3.0	1.9	4.7
	Pharyngitis streptococcal (10034839)	8	1.5	0.6	2.8	13	2.0	1.1	3.4	8	1.4	0.6	2.8	15	2.3	1.3	3.7
	Pharyngotonsillitis (10049140)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	6	1.1	0.4	2.3	0	0.0	0.0	0.6
	Pneumonia (10035664)	8	1.5	0.6	2.8	14	2.1	1.2	3.5	7	1.3	0.5	2.6	19	2.9	1.7	4.5
	Pneumonia bacterial (10060946)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Pneumonia mycoplasmal (10035724)	0	0.0	0.0	0.7	4	0.6	0.2	1.6	1	0.2	0.0	1.0	3	0.5	0.1	1.3
	Pneumonia viral (10035737)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pseudomonas infection (10061471)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Rash pustular (10037888)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Respiratory syncytial virus bronchiolitis (10038718)	4	0.7	0.2	1.9	2	0.3	0.0	1.1	3	0.5	0.1	1.6	2	0.3	0.0	1.1
	Respiratory syncytial virus infection (10061603)	7	1.3	0.5	2.6	8	1.2	0.5	2.4	8	1.4	0.6	2.8	7	1.1	0.4	2.2
	Respiratory tract infection (10062352)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	3	0.5	0.1	1.6	0	0.0	0.0	0.6
	Respiratory tract infection viral (10062106)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Rhinitis (10039083)	4	0.7	0.2	1.9	4	0.6	0.2	1.6	5	0.9	0.3	2.1	3	0.5	0.1	1.3
	Roseola (10039222)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Rotavirus infection (10067470)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Scarlet fever (10039587)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Sinusitis (10040753)	16	2.9	1.7	4.7	15	2.3	1.3	3.7	19	3.4	2.1	5.2	24	3.7	2.4	5.4
	Sinusitis bacterial (10060841)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Skin candida (10054152)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Skin infection (10040872)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Staphylococcal infection (10058080)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	0	0.0	0.0	0.7	3	0.5	0.1	1.3
	Streptococcal infection (10061372)	1	0.2	0.0	1.0	3	0.5	0.1	1.3	1	0.2	0.0	1.0	4	0.6	0.2	1.6
	Subcutaneous abscess (10042343)	0	0.0	0.0	0.7	4	0.6	0.2	1.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Tinea capitis (10043866)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Tinea infection (10060889)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tonsillitis (10044008)	6	1.1	0.4	2.4	4	0.6	0.2	1.6	8	1.4	0.6	2.8	3	0.5	0.1	1.3
	Tonsillitis streptococcal (10044013)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Tooth infection (10048762)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tracheitis (10044302)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tracheobronchitis viral (10061556)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Upper respiratory tract infection (10046306)	121	22.0	18.6	25.7	122	18.6	15.7	21.8	127	22.7	19.3	26.4	106	16.1	13.4	19.2
	Urinary tract infection (10046571)	2	0.4	0.0	1.3	6	0.9	0.3	2.0	6	1.1	0.4	2.3	5	0.8	0.2	1.8
	Vaginal infection (10046914)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Varicella (10046980)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Viral infection (10047461)	26	4.7	3.1	6.9	28	4.3	2.9	6.1	26	4.6	3.1	6.7	28	4.3	2.9	6.1

		Q-QIV								F-QIV							
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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Viral pharyngitis (10047473)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	2	0.4	0.0	1.3	2	0.3	0.0	1.1
	Viral rash (10047476)	16	2.9	1.7	4.7	2	0.3	0.0	1.1	12	2.1	1.1	3.7	6	0.9	0.3	2.0
	Viral tonsillitis (10047480)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Viral upper respiratory tract infection (10047482)	13	2.4	1.3	4.0	5	0.8	0.2	1.8	13	2.3	1.2	3.9	9	1.4	0.6	2.6
	Vulvovaginitis (10047794)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Wound infection (10048038)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Animal bite (10002515)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Arthropod bite (10003399)	3	0.5	0.1	1.6	4	0.6	0.2	1.6	0	0.0	0.0	0.7	4	0.6	0.2	1.6
	Burns first degree (10006797)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Burns second degree (10006802)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Clavicle fracture (10009245)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Concussion (10010254)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Contusion (10050584)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	2	0.4	0.0	1.3	2	0.3	0.0	1.1
	Corneal abrasion (10010984)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Craniocerebral injury (10070976)	1	0.2	0.0	1.0	3	0.5	0.1	1.3	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Exposure to communicable disease (10049711)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Exposure to toxic agent (10053487)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Face injury (10050392)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Fall (10016173)	0	0.0	0.0	0.7	3	0.5	0.1	1.3	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Foreign body (10070245)	0	0.0	0.0	0.7	3	0.5	0.1	1.3	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Hand fracture (10019114)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Head injury (10019196)	5	0.9	0.3	2.1	6	0.9	0.3	2.0	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Humerus fracture (10020462)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Injury (10022116)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Joint dislocation (10023204)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Joint injury (10060820)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Laceration (10023572)	4	0.7	0.2	1.9	12	1.8	0.9	3.2	0	0.0	0.0	0.7	8	1.2	0.5	2.4

		Q-QIV								F-QIV							
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				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Ligament sprain (10024453)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Limb crushing injury (10064031)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Limb injury (10061225)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Lip injury (10055082)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	2	0.3	0.0	1.1
	Mouth injury (10049294)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Multiple injuries (10028224)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Procedural pain (10064882)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Radial head dislocation (10073749)	0	0.0	0.0	0.7	3	0.5	0.1	1.3	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Rib fracture (10039117)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Road traffic accident (10039203)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Skin abrasion (10064990)	0	0.0	0.0	0.7	4	0.6	0.2	1.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Splinter (10041662)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Thermal burn (10053615)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tooth injury (10044043)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Ulna fracture (10045375)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Upper limb fracture (10061394)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Vaccination complication (10046861)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Wound (10052428)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Wound complication (10053692)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Investigations (10022891)	Blood carbon monoxide (10005406)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Blood lead increased (10005642)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Body temperature increased (10005911)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Cardiac murmur (10007586)	1	0.2	0.0	1.0	3	0.5	0.1	1.3	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Heart rate increased (10019303)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Weight increased (10047899)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Metabolism and nutrition disorders (10027433)	Abnormal weight gain (10000188)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Breast milk substitute intolerance (10072187)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Decreased appetite (10061428)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	3	0.5	0.1	1.6	3	0.5	0.1	1.3
	Dehydration (10012174)	5	0.9	0.3	2.1	4	0.6	0.2	1.6	2	0.4	0.0	1.3	4	0.6	0.2	1.6
	Failure to thrive (10016165)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Feeding disorder (10061148)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Feeding disorder of infancy or early childhood (10016318)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Hyponatraemia (10021036)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Lactose intolerance (10023681)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Obesity (10029883)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Overweight (10033307)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pica (10035001)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
Musculoskeletal and connective tissue disorders (10028395)	Arthralgia (10003239)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Back pain (10003988)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Blount's disease (10072255)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Flank pain (10016750)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Foot deformity (10061159)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Growing pains (10018745)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Growth retardation (10053759)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Head deformity (10061199)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hypermobility syndrome (10020677)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Joint swelling (10023232)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Knee deformity (10062061)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Musculoskeletal pain (10028391)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pain in extremity (10033425)	3	0.5	0.1	1.6	2	0.3	0.0	1.1	1	0.2	0.0	1.0	3	0.5	0.1	1.3
	Synovial cyst (10042858)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Tenosynovitis (10043261)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Torticollis (10044074)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	B precursor type acute leukaemia (10003890)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Haemangioma (10018814)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Melanocytic naevus (10027145)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Skin papilloma (10040907)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	4	0.6	0.2	1.6

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.7	5	0.8	0.2	1.8	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Fine motor delay (10066088)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Gross motor delay (10069118)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Hemiplegia (10019468)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Language disorder (10074869)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Motor developmental delay (10070302)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Presyncope (10036653)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Seizure (10039906)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Sensory integrative dysfunction (10048871)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Speech disorder (10041466)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Speech disorder developmental (10041467)	2	0.4	0.0	1.3	5	0.8	0.2	1.8	1	0.2	0.0	1.0	3	0.5	0.1	1.3
	Tremor (10044565)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Pregnancy, puerperium and perinatal conditions (10036585)	Cephalhaematoma (10008014)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Psychiatric disorders (10037175)	Abnormal behaviour (10061422)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Autism spectrum disorder (10063844)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Eating disorder (10014062)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Head banging (10019191)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Insomnia (10022437)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Irritability (10022998)	3	0.5	0.1	1.6	3	0.5	0.1	1.3	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Libido disorder (10061221)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Middle insomnia (10027590)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Onychophagia (10057342)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Phonological disorder (10034925)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Sleep disorder (10040984)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Renal and urinary disorders (10038359)	Calculus urinary (10007027)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dysuria (10013990)	0	0.0	0.0	0.7	4	0.6	0.2	1.6	1	0.2	0.0	1.0	3	0.5	0.1	1.3
	Enuresis (10014928)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Pollakiuria (10036018)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Urinary incontinence (10046543)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Urinary tract disorder (10046566)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8

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Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Urine odour abnormal (10057135)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Reproductive system and breast disorders (10038604)	Balanoposthitis (10004078)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Genital erythema (10054816)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Genital labial adhesions (10064162)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	4	0.7	0.2	1.8	1	0.2	0.0	0.8
	Genital rash (10018175)	5	0.9	0.3	2.1	0	0.0	0.0	0.6	4	0.7	0.2	1.8	2	0.3	0.0	1.1
	Gynaecomastia (10018800)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Penile adhesion (10059636)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Pruritus genital (10037093)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Testicular retraction (10043348)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Vaginal discharge (10046901)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Adenoidal hypertrophy (10001229)	1	0.2	0.0	1.0	2	0.3	0.0	1.1	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Asthma (10003553)	3	0.5	0.1	1.6	7	1.1	0.4	2.2	6	1.1	0.4	2.3	15	2.3	1.3	3.7
	Bronchial hyperreactivity (10066091)	8	1.5	0.6	2.8	4	0.6	0.2	1.6	5	0.9	0.3	2.1	7	1.1	0.4	2.2
	Bronchospasm (10006482)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Cough (10011224)	21	3.8	2.4	5.8	25	3.8	2.5	5.6	29	5.2	3.5	7.4	35	5.3	3.7	7.3
	Dyspnoea (10013968)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Epistaxis (10015090)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	2	0.3	0.0	1.1
	Hypoxia (10021143)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Lower respiratory tract congestion (10075565)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Nasal congestion (10028735)	11	2.0	1.0	3.6	3	0.5	0.1	1.3	8	1.4	0.6	2.8	7	1.1	0.4	2.2
	Nasal discomfort (10052437)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Oropharyngeal pain (10068319)	1	0.2	0.0	1.0	3	0.5	0.1	1.3	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pneumonitis (10035742)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pulmonary congestion (10037368)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Respiratory disorder (10038683)	3	0.5	0.1	1.6	4	0.6	0.2	1.6	7	1.3	0.5	2.6	6	0.9	0.3	2.0
	Respiratory distress (10038687)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rhinitis allergic (10039085)	9	1.6	0.8	3.1	5	0.8	0.2	1.8	5	0.9	0.3	2.1	7	1.1	0.4	2.2
	Rhinorrhoea (10039101)	5	0.9	0.3	2.1	3	0.5	0.1	1.3	8	1.4	0.6	2.8	8	1.2	0.5	2.4
	Sinus congestion (10040742)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6

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		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
	Sinus disorder (10062244)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	2	0.3	0.0	1.1
	Sleep apnoea syndrome (10040979)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	2	0.4	0.0	1.3	1	0.2	0.0	0.8
	Sneezing (10041232)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Snoring (10041235)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Tonsillar hypertrophy (10044003)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	3	0.5	0.1	1.3
	Upper-airway cough syndrome (10070488)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Wheezing (10047924)	9	1.6	0.8	3.1	11	1.7	0.8	3.0	7	1.3	0.5	2.6	5	0.8	0.2	1.8
Skin and subcutaneous tissue disorders (10040785)	Angioedema (10002424)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Blister (10005191)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Cafe au lait spots (10006926)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Dermal cyst (10012426)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Dermatitis (10012431)	5	0.9	0.3	2.1	3	0.5	0.1	1.3	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Dermatitis atopic (10012438)	2	0.4	0.0	1.3	5	0.8	0.2	1.8	9	1.6	0.7	3.0	7	1.1	0.4	2.2
	Dermatitis contact (10012442)	2	0.4	0.0	1.3	1	0.2	0.0	0.8	4	0.7	0.2	1.8	3	0.5	0.1	1.3
	Dermatitis diaper (10012444)	20	3.6	2.2	5.6	11	1.7	0.8	3.0	16	2.9	1.6	4.6	7	1.1	0.4	2.2
	Dry skin (10013786)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Ecchymosis (10014080)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Eczema (10014184)	3	0.5	0.1	1.6	1	0.2	0.0	0.8	14	2.5	1.4	4.2	3	0.5	0.1	1.3
	Eczema nummular (10014201)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Erythema (10015150)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Erythema multiforme (10015218)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Hand dermatitis (10058898)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Idiopathic urticaria (10021247)	0	0.0	0.0	0.7	2	0.3	0.0	1.1	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Ingrowing nail (10022013)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Keratosis pilaris (10066295)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	1	0.2	0.0	0.8
	Miliaria (10027627)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Nail disorder (10028694)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Neurodermatitis (10029263)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Petechiae (10034754)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Prurigo (10037083)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Rash (10037844)	8	1.5	0.6	2.8	6	0.9	0.3	2.0	3	0.5	0.1	1.6	11	1.7	0.8	3.0

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
	Rash erythematous (10037855)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rash generalised (10037858)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Rash macular (10037867)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Skin fissures (10040849)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Skin lesion (10040882)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Solar urticaria (10041307)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Urticaria (10046735)	7	1.3	0.5	2.6	10	1.5	0.7	2.8	4	0.7	0.2	1.8	6	0.9	0.3	2.0
	Urticaria papular (10046750)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Social circumstances (10041244)	Sexual abuse (10040461)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Surgical and medical procedures (10042613)	Adenoidectomy (10001230)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Umbilical hernia repair (10045462)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Vascular disorders (10047065)	Haematoma (10018852)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Kawasaki's disease (10023320)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pallor (10033546)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 130 Percentage of subjects reporting the occurrence of potential immune-mediated diseases (pIMDs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire study period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one symptom		0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Skin and subcutaneous tissue disorders (10040785)	Erythema multiforme (10015218)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Vascular disorders (10047065)	Kawasaki's disease (10023320)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
UNPRIM = Unprimed subjects
PRIM = Primed subjects
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 131 Percentage of subjects reporting the occurrence of serious adverse events (SAEs) classified by MedDRA Primary System Organ Class and Preferred Term during the entire study period by priming status (Total vaccinated cohort)

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		8	1.5	0.6	2.8	14	2.1	1.2	3.5	13	2.3	1.2	3.9	8	1.2	0.5	2.4
Gastrointestinal disorders (10017947)	Constipation (10010774)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Intussusception (10022863)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
General disorders and administration site conditions (10018065)	Developmental delay (10012559)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Infections and infestations (10021881)	Abscess (10000269)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Bronchiolitis (10006448)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	2	0.4	0.0	1.3	0	0.0	0.0	0.6
	Cellulitis (10007882)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Croup infectious (10011416)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Gastroenteritis (10017888)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	2	0.3	0.0	1.1
	Gastroenteritis rotavirus (10017913)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Groin abscess (10050269)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Lower respiratory tract infection (10024968)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Otitis media acute (10033079)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Pharyngitis (10034835)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Pneumonia (10035664)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Respiratory syncytial virus bronchiolitis (10038718)	2	0.4	0.0	1.3	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Respiratory syncytial virus infection (10061603)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Staphylococcal abscess (10041917)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Urinary tract infection (10046571)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Injury, poisoning and procedural complications (10022117)	Accidental exposure to product (10073317)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Concussion (10010254)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Craniocerebral injury (10070976)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Multiple injuries (10028224)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6

		Q-QIV								F-QIV							
		UNPRIM N = 550				PRIM N = 657				UNPRIM N = 560				PRIM N = 657			
				95% CI				95% CI				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Metabolism and nutrition disorders (10027433)	Dehydration (10012174)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	1	0.2	0.0	1.0	2	0.3	0.0	1.1
	Failure to thrive (10016165)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Hyponatraemia (10021036)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Neoplasms benign, malignant and unspecified (incl cysts and polyps) (10029104)	B precursor type acute leukaemia (10003890)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
Nervous system disorders (10029205)	Febrile convulsion (10016284)	0	0.0	0.0	0.7	5	0.8	0.2	1.8	3	0.5	0.1	1.6	1	0.2	0.0	0.8
	Hemiplegia (10019468)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	0	0.0	0.0	0.7	1	0.2	0.0	0.8
	Seizure (10039906)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Renal and urinary disorders (10038359)	Calculus urinary (10007027)	0	0.0	0.0	0.7	0	0.0	0.0	0.6	1	0.2	0.0	1.0	0	0.0	0.0	0.6
Respiratory, thoracic and mediastinal disorders (10038738)	Asthma (10003553)	1	0.2	0.0	1.0	1	0.2	0.0	0.8	1	0.2	0.0	1.0	0	0.0	0.0	0.6
	Hypoxia (10021143)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
	Pneumonitis (10035742)	1	0.2	0.0	1.0	0	0.0	0.0	0.6	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Social circumstances (10041244)	Sexual abuse (10040461)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6
Vascular disorders (10047065)	Kawasaki's disease (10023320)	0	0.0	0.0	0.7	1	0.2	0.0	0.8	0	0.0	0.0	0.7	0	0.0	0.0	0.6

Q-QIV = Flu Q-QIV
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At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
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12. STUDY REPORT AUTHORS /CONTRIBUTING AUTHORS

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13. SERIOUS ADVERSE EVENTS / OTHER SIGNIFICANT ADVERSE EVENTS

13.1. SAE Listing(s)

Table 132 Listing of SAEs reported during the entire study period (Total vaccinated cohort)

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
Q-QIV	(b) (6)	NA	17	F	Kawasaki disease	Kawasaki's disease	Vascular disorders	HO	1	93	.	.	N	Recovering/resolving
			17		Urinary tract infection	Urinary tract infection	Infections and infestations	HO	1	94	16	2	N	Recovered/resolved
		NA	25	M	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	5	1	3	N	Recovered/resolved
		NA	18	M	Hypoxia	Hypoxia	Respiratory, thoracic and mediastinal disorders	HO	1	76	3	3	N	Recovered/resolved
		NA	28	M	Acute gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	83	4	2	N	Recovered/resolved
			29		Dehydration	Dehydration	Metabolism and nutrition disorders	HO	1	85	2	2	N	Recovered/resolved
			29		Hyponatremia	Hyponatraemia	Metabolism and nutrition disorders	HO	1	85	2	2	N	Recovered/resolved
		NA	12	M	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	2	1	12	2	N	Recovered/resolved
		NA	26	M	Head concussion	Concussion	Injury, poisoning and procedural complications	ER	1	88	11	2	N	Recovered/resolved
			26		Closed head injury	Craniocerebral injury	Injury, poisoning and procedural complications	ER	1	88	11	2	N	Recovered/resolved
		NA	36	F	Sexual assault, alleged.	Sexual abuse	Social circumstances	ER	1	66	6	1	N	Recovered/resolved
		NA	14	F	Bronchiolitis due to respiratory syncytial virus	Respiratory syncytial virus bronchiolitis	Infections and infestations	HO	2	44	10	2	N	Recovered/resolved
		NA	27	M	Fever seizure	Febrile convulsion	Nervous system disorders	ER	1	88	1	3	N	Recovered/resolved

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
	(b) (6)	NA	12	M	Right abdominal wall cellulitis/worsening	Cellulitis	Infections and infestations	HO	1	0	21	3	N	Recovered/resolved
			12		Right anterior groin abscess/worsening	Groin abscess	Infections and infestations	HO	1	0	21	3	N	Recovered/resolved
		NA	19	M	Croup	Croup infectious	Infections and infestations	HO	1	31	.	2	N	Recovering/resolving
		NA	21	F	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	168	1	3	N	Recovered/resolved
		NA	22	M	Multisystem trauma	Multiple injuries	Injury, poisoning and procedural complications	HO	2	82	27	2	N	Recovered/resolved
		NA	11	M	Lower respiratory airway disease	Lower respiratory tract infection	Infections and infestations	HO	2	71	8	3	N	Recovered/resolved
			11		Pneumonitis with perihilar markings	Pneumonitis	Respiratory, thoracic and mediastinal disorders	HO	2	71	8	3	N	Recovered/resolved
			11		Respiratory syncytial virus bronchiolitis	Respiratory syncytial virus bronchiolitis	Infections and infestations	HO	2	71	8	3	N	Recovered/resolved
		NA	13	F	Asthma	Asthma	Respiratory, thoracic and mediastinal disorders	HO	2	62	72	2	N	Recovered/resolved
		NA	32	F	Pneumonia in left lung	Pneumonia	Infections and infestations	HO	1	161	3	3	N	Recovered/resolved
		NA	13	F	Staphylococcus aureus abscess	Staphylococcal abscess	Infections and infestations	HO	1	2	19	3	N	Recovered/resolved
		NA	37	M	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	106	1	2	N	Recovered/resolved
		NA	19	M	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	50	1	2	N	Recovered/resolved
		NA	29	F	Ingestion of medication	Accidental exposure to product	Injury, poisoning and procedural complications	HO	1	54	2	3	N	Recovered/resolved
		NA	35	M	Asthma exacerbation	Asthma	Respiratory, thoracic and mediastinal disorders	HO	1	120	7	3	N	Recovered/resolved
		NA	11	F	Dehydration	Dehydration	Metabolism and nutrition disorders	HO	2	115	4	3	N	Recovered/resolved

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
F-QIV	(b) (6)	NA	31	F	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	2	74	1	1	N	Recovered/resolved
		NA	15	F	Urolithiasis	Calculus urinary	Renal and urinary disorders	HO	2	29	64	3	N	Recovered/resolved
			16		Urinary tract infection	Urinary tract infection	Infections and infestations	HO	2	77	9	2	N	Recovered/resolved
		NA	27	F	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	25	5	2	N	Recovered/resolved
			27		Acute otitis media	Otitis media acute	Infections and infestations	HO	1	25	11	2	N	Recovered/resolved
			27		Pharyngitis	Pharyngitis	Infections and infestations	HO	1	22	15	2	N	Recovered/resolved
		NA	26	F	Worsening constipation	Constipation	Gastrointestinal disorders	HO	1	104	9	3	N	Recovered/resolved
		NA	32	M	Pre-B cell acute lymphoblastic leukemia	B precursor type acute leukaemia	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	HO	1	125	.	3	N	Not recovered/not resolved
		NA	35	F	Respiratory syncytial virus	Respiratory syncytial virus infection	Infections and infestations	HO	1	81	17	3	N	Recovered/resolved
		NA	18	M	Acute asthma exacerbation	Asthma	Respiratory, thoracic and mediastinal disorders	HO	2	126	3	2	N	Recovered/resolved
		NA	16	M	Febrile convulsions (simple), unspecified	Febrile convulsion	Nervous system disorders	HO	2	80	2	2	N	Recovered/resolved
		NA	26	F	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	1	178	1	3	N	Recovered/resolved
		NA	8	F	Failure to thrive	Failure to thrive	Metabolism and nutrition disorders	HO	2	47	.	3	N	Not recovered/not resolved
		NA	12	F	Multiple abscesses	Abscess	Infections and infestations	HO	1	6	28	3	N	Recovered/resolved
			12		Right thigh cellulitis	Cellulitis	Infections and infestations	HO	1	5	29	3	N	Recovered/resolved

Group	Sub. No.	Case Id	Age at onset (Month)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
	(b) (6)		12		Left thigh cellulitis	Cellulitis	Infections and infestations	HO	1	5	29	3	N	Recovered/resolved
		NA	36	M	Developmental delay	Developmental delay	General disorders and administration site conditions	MD	1	76	.	2	N	Not recovered/not resolved
			36		Hemiplegia	Hemiplegia	Nervous system disorders	MD	1	76	.	2	N	Not recovered/not resolved
		NA	10	M	Intussusception	Intussusception	Gastrointestinal disorders	HO	2	7	2	3	N	Recovered/resolved
		NA	37	F	Rotavirusgastroenteritis	Gastroenteritis rotavirus	Infections and infestations	HO	2	111	6	3	N	Recovered/resolved
		NA	12	M	Bronchiolitis	Bronchiolitis	Infections and infestations	HO	1	1	14	3	N	Recovered/resolved
		NA	19	F	Seizure	Seizure	Nervous system disorders	HO	2	103	10	2	N	Recovered/resolved
		NA	14	F	Febrile seizure	Febrile convulsion	Nervous system disorders	ER	2	39	1	3	N	Recovered/resolved
		NA	21	M	Dehydration	Dehydration	Metabolism and nutrition disorders	HO	1	112	7	3	N	Recovered/resolved
			21		Gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	112	7	3	N	Recovered/resolved
		NA	30	F	Gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	79	7	3	N	Recovered/resolved
		NA	17	M	Dehydration	Dehydration	Metabolism and nutrition disorders	HO	1	126	2	3	N	Recovered/resolved
		NA	16	M	Dehydration	Dehydration	Metabolism and nutrition disorders	HO	2	72	6	3	N	Recovered/resolved

Q-QIV = Flu Q-QIV
F-QIV = Fluzone Quadrivalent
NA = Not Applicable (SAEs available only in Clinical Data)
MED = Medically attended visit

13.2. Clinical Narratives for SAEs

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Unblinded Report – With Suspect Products and Serious and Non-Serious Events

Study Number: 201234

Study Center ID: 210113

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Bronchiolitis

Non-Serious Events:

Narrative: This 12-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 1 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 bronchiolitis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with prednisolone sodium phosphate (Orapred) and salbutamol sulfate (Accuneb). The outcome of bronchiolitis was recovered/resolved on 4th December 2014.

The investigator considered that there was no reasonable possibility that the bronchiolitis may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Chest x-ray done (b) (6): Prominent peribronchial markings, no focal lung disease identified. Respiratory Infectious Disease Panel by PCR (RIDPP) done (b) (6) Negative.

Investigator Comment:
Subject presented to PCP on (b) (6) /o nasal congestion, rhinorrhea, cough and wheeze. Diagnosed with left acute otitis media, URI and wheeze. Presented to ER that evening for increased respiratory rate and fever. Diagnosed with bronchiolitis and D/C to home. Again went to PCP on (b) (6), at that point was lethargic and had decreased PO intake, and was sent back to ER. Was admitted for IVF and observation. D/C to home on (b) (6) in good condition.

Study Number: 201234

Study Center ID: 210113

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

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Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 3-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included febrile convulsion. Concomitant products included diazepam.

On (b) (6) 08:00, 106 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The outcome of febrile seizure was recovered/resolved on (b) (6) 08:02.

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Subject had Abdominal Xray, Chest Xray Strep A throat screen, Urinalysis with reflex microbilogy and ALL came back Normal and WNL on (b) (6) Diagnostic results (unless otherwise stated, normal values were not provided): On (b) (6), Blood glucose result was 77 mg (normal low: 60, normal high: 100).

Investigator Text:
Per protocol and sponsor requiremnets this event is a RMP and will be reported as SAE. Subject presented to ER on (b) (6) after seizure episode lasting 2 minutes. Subject had previous suspected episode on 2/17/15, however per PCP and Neuro consult episode diagnosed as Vasovagal episode. Subject does have prior febrile seizure history times 3 from 12/12-03/13. For this reported episode subject also complans of abdominal pain, has had chronic fever episodes and Viral syndrome symptoms. Subject was given at Neuro consult and follow up on (b) (6) a prescription of Diazepam and parent confirms the as needed "PRN" usage. Subject was in ER for less than 3 hours had several tests and all were normal. Subject left ER in good/stable condition. Subject f/u with PCP on (b) (6) with no further episodes. Subject completed study on (b) (6) with no further episodes. No further information will be needed.

Study Number: 201234

Study Center ID: 210113

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Constipation

Non-Serious Events:

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Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

Concurrent medical conditions included constipation.

On (b) (6), 104 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 constipation aggravated. Serious criteria included hospitalization. The subject was treated with macrogol (Miralax), electrolytes nos + macrogol (Golytely), dimeticone, activated (Mylicon), zinc oxide (Zinc Oxide Ointment), ondansetron (Zofran) and sodium phosphate dibasic + sodium phosphate monobasic (Fleet Pediatric Enema). The outcome of constipation aggravated was recovered/resolved on (b) (6).

The investigator considered that there was no reasonable possibility that the constipation aggravated may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: 1. Abdominal x-ray (b) (6): A moderate amount of stool is present throughout the colon. 2. Abdominal x-ray (b) (6): Enteric tube tip is in the stomach. 3. Abdominal x-ray (b) (6) at 14:55: No residual stool is identified in the colon. 4. Abdominal x-ray (b) (6) at 16:13: Small amount of stool in the colon.

Investigators Text:
Subject presented to ED on (b) (6) with worsening constipation and abdominal pain. Admitted to Almost Home observational unit for placement of NG tube with GoLytely administration for bowel cleanout. Subject discharged home on (b) (6) in good condition.

Study Number: 201234

Study Center ID: 210113

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: B precursor type acute leukaemia

Non-Serious Events:

Narrative: This 2-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included lymphadenopathy.

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On (b) (6), 125 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 precursor b-lymphoblastic leukemia acute. Serious criteria included hospitalization and GSK medically significant. The subject was treated with vincristine sulfate (Oncovin), vincristine, dexamethasone, pegaspargase and cytarabine. The outcome of precursor b-lymphoblastic leukemia acute was not recovered/not resolved.

The investigator considered that there was no reasonable possibility that the precursor b-lymphoblastic leukemia acute may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Chest Xray performed on (b) (6), EKG performed on (b) (6), Echocardiogram performed on (b) (6) All were Normal. Bone marrow aspiration was done on (b) (6) and revealed numerous blast cells Diagnostic results (unless otherwise stated, normal values were not provided): On (b) (6), Haematocrit result was 25.1 % (normal low: 32, normal high: 42), Haemoglobin result was 8.1 g/dL (normal low: 11.5, normal high: 14.5), Platelet count result was 117 (normal low: 140, normal high: 440), Red blood cell sedimentation rate result was 45 (normal low: 0.00, normal high: 13), Reticulocyte count result was 4.2 % (normal low: 0.3, normal high: 1.5) and White blood cell count result was 20.5 (normal low: 4, normal high: 12).

Investigator Comments:
Subject admitted to hospital on (b) (6) for symptoms concerning for leukemia, including but not limited to Lymphadenopathy which presented on (b) (6). Leukemia was confirmed by bone marrow aspiration result on (b) (6). Subject underwent induction chemotherapy during hospital stay. He was discharged home on (b) (6) in good condition. Further details of event are pending receipt of hospital records. Subject had lymphadenopathy for 1 day prior to hospital visit on (b) (6). Subject saw PCP on (b) (6) and due to the abnormal size of lymph nodes subject referred to ER. Subject was diagnosed with pre B cell acute lymphoblastic leukemia. Subject was in hospital (b) (6) and had SC implanted central venous catheter port on (b) (6) for the administration of chemotherapy. Chemotherapy tx is antineoplastic Oncovin and it was administered and chemo will continue for the next 3 years.
Subject has had numerous hospital visits as he does get his chem tx in hospital. Subject has been found to have several AEs due to SAE and the treatment for it. Numerous meds also given for treatment of SAE and AEs. Subjects parent states subject is doing well "considerably speaking" and subject has completed the study in stable condition.

Study Number: 201234

Study Center ID: 210113

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Respiratory syncytial virus infection

Non-Serious Events:

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Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

Concomitant products included oseltamivir phosphate (Tamiflu), paracetamol (Tylenol) and ibuprofen (Motrin).

On (b) (6), 81 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 respiratory syncytial virus infection. Serious criteria included hospitalization. The subject was treated with ketorolac trometamol (Toradol), ipratropium bromide + salbutamol sulfate (Duoneb), paracetamol (Tylenol), sodium chloride, epinephrine hydrochloride (Vaponefrin) and salbutamol (Ventolin Hfa). The outcome of respiratory syncytial virus infection was recovered/resolved on 10th February 2015.

The investigator considered that there was no reasonable possibility that the respiratory syncytial virus infection may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: (b) (6) Respiratory Infectious Disease Panel positive for RSV; (b) (6): Rapid Flu for Influenza A/B negative for Influenza A and B; (b) (6): chest x-ray with no radiographic abnormality identified.

Investigator Comment:
Subject presented to ED on (b) (6) with c/o fever, congestion, cough and wheezing x 2 days. Suspected to have bronchiolitis. Rapid flu test was negative on (b) (6). Subject was admitted to Almost Home observational unit for close observation, supportive care and further evaluation. Respiratory Infectious Disease Panel was positive for RSV on (b) (6). Subject was discharged home on (b) (6) in good condition.

Study Number: 201234

Study Center ID: 210149

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Respiratory syncytial virus bronchiolitis, Pneumonitis, Lower respiratory tract infection

Non-Serious Events:

Narrative: This 11-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 71 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed

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severe - grade 3 respiratory syncytial virus bronchiolitis. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included severe - grade 3 pneumonitis on (b) (6) with serious criteria of hospitalization and severe - grade 3 lower respiratory tract infection on (b) (6) with serious criteria of hospitalization and GSK medically significant. The subject was treated with ipratropium bromide + salbutamol. The outcome of respiratory syncytial virus bronchiolitis was recovered/resolved on 29th January 2015. The outcome(s) of the additional event(s) included pneumonitis (recovered/resolved on 29th January 2015) and lower respiratory tract infection (recovered/resolved on 29th January 2015).

The investigator considered that there was no reasonable possibility that the respiratory syncytial virus bronchiolitis, pneumonitis and lower respiratory tract infection may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Respiratory Viral Panel by PCR - RSV detected on (b) (6) Chest X-ray on (b) (6) with findings of lower airway disease and pneumonitis with perihilar markings.

Investigator Text:
Subject presented to ER on (b) (6) with a 3 day history of fever and clear rhinorrhea, a 2 day history of difficulty breathing and severe cough with cough paroxysms at home. The subject has not required previous hospitalizations for hypoxia or difficulty breathing. Subject has a family history of reactive airway disease and asthma in his mother. Subject admitted to hospital from (b) (6). The initial lab testing indicated the presence of RSV (Respiratory Syncytial Virus), thus making his diagnosis RSV bronchiolitis. His CXR was consistent with a viral lower respiratory infection. Subject initially required oxygen to maintain saturation while awake and while asleep. The subject was off oxygen for greater than 16 hours prior to discharge, even throughout sleeping at night and during naps. Parents were thus encouraged to continue bulb suction and nasal saline at home to maintain a clear airway.

Study Number: 201234

Study Center ID: 210149

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Asthma

Non-Serious Events:

Narrative: This 15-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

Concomitant products included azithromycin and ceftriaxone sodium (Rocephin).

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On (b) (6), 62 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 asthma. Serious criteria included hospitalization. The subject was treated with salbutamol (Albuterol) and prednisone. The outcome of asthma was recovered/resolved on 15th May 2015.

The investigator considered that there was no reasonable possibility that the asthma may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Chest X ray on (b) (6) showed some perihilar markings and questionable small infiltrate in the right lower lobe. Negative Influenza A and B testing on (b) (6). Negative for respiratory syncytial virus on (b) (6).

INVESTIGATOR TEXT
Subject showed signs of runny nose, postnasal drip, and cough on 5/8/15. Subject began to have increased progressive wheezing and tachypnea on (b) (6) and was brought in to ER. Oxygen saturating in 86 to 88 percent. RSV and influenza negative. Subject was kept in hospital for observation. Remained well-hydrated during hospitalization, responded well to nebulizers. Discharged in stable condition on (b) (6). Subject fully recovered on 5/15/15.

Study Number: 201234

Study Center ID: 210151

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 2-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6) 17:00, 2 years and 5 days after receiving Flu Q-QIV vs Fluzone Quadrivalent the subject developed severe - grade 3 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The subject was treated with oseltamivir phosphate and ibuprofen. The outcome of febrile seizure was recovered/resolved on 7th December 2014 17:05.

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: (b) (6) Nasopharyngeal swab positive for influenza A.

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Investigator comments : Subject'ss mother notified the site today of an event that took place on (b) (6). Subject had a febrile seizure at 17:00. Subject's mother reported that the subject's grandmother said that subject was "turning blue" so she started performing "CPR." Mother did not witness the event. Subject vomited and was taken to the ER. At the ER, subject was diagnosed with influenza. Mother said that she believed the subject's temperature was 105 F, but she did not write it down. She reports that subject's temperatures were normal leading up to the fever on (b) (6). Subject was at the ER from 18:00-20:00 on (b) (6) and was prescribed Tamiflu. Influenza resolved and subject has been doing well since, per mother. Medical records pending.
Medical records received. Febrile seizure, no asphyxiation only postictal. Child was positive for influenza per nasopharyngeal swab. Previously reported SAE items of asphyxiation, emesis and influenza have been removed. Subject was not hospitalized. Febrile Seizure is reported as an SAE per protocol because it is potential risk in the risk management plan. Febrile seizure and ER visit was on (b) (6), not (b) (6) per medical records.

Study Number: 201234

Study Center ID: 210152

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included febrile seizure. Concomitant products included HEPATITIS A VACCINE.

On (b) (6), 178 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The subject was treated with paracetamol (Tylenol (Acetaminophen)) and ibuprofen (Motrin (Ibuprofen)). The outcome of febrile seizure was recovered/resolved on (b) (6).

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Comment:
Subject presented to the ER 6 months post vaccination after parent reported she was "having a seizure". States head was turned to side with eyes open, arms twitching, and breathing irregularly. Reported that it lasted less than 5 minutes. Temperature was immediately taken and was reported as 106F (unknown

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route). Subject given ibuprofen and was sleepy. Subject was back to baseline when medics arrived. ER ordered urinalysis and urine culture. Results not known. Parent reports that subject has a prior history of febrile seizure X 1 on 20Jun2014. Discharged from ER, with normal temperature and neurologically intact. Although the event of a febrile seizure is not considered serious in the clinical field, the protocol has mandated that this be reported as a Serious Adverse Event.

Study Number: 201234

Study Center ID: 210153

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Failure to thrive

Non-Serious Events:

Narrative: This 9-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included esophageal reflux.

On (b) (6), 47 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 failure to thrive. Serious criteria included hospitalization and GSK medically significant. The outcome of failure to thrive was not recovered/not resolved.

The investigator considered that there was no reasonable possibility that the failure to thrive may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Comment:
Subject came in on (b) (6) to the clinic and weight was 6.35 kg then came in again on (b) (6) weight was 6.29 kg and again on (b) (6) weight was 6.33 kg. The weight had been in that range for the last 4-5 months. Per moms report there was a history of esophageal reflux form age 0-1 month. Also noticed recent illness of otitis media and Utricria. was on Antibiotic for otitis media and steroid for Utricria. symptoms of failure to thrive were limited time breast feeding, declines solids, refuses bottles, does tolerate some thin cereals. admitted to hospital on (b) (6) and NG tube was placed with bolus gravity breast milk given. some labs were drawn will update when information is available, patient had gained weight in hospital. working with occupational therapy to improve feeding habits. patient was discharged from hospital on (b) (6) with NG still in and working with out patient occupational therapy for 1 month

Study Number: 201234

Study Center ID: 210155

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Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Hypoxia

Non-Serious Events:

Narrative: This 18-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

Concurrent medical conditions included pneumonia. Concomitant products included paracetamol (Tylenol).

On (b) (6) 05:34, 76 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 hypoxia. Serious criteria included hospitalization and GSK medically significant. The subject was treated with amoxicillin. The outcome of hypoxia was recovered/resolved on 8th January 2015 13:52.

The investigator considered that there was no reasonable possibility that the hypoxia may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Chest X-ray performed on (b) (6) revealed "Diffuse bilateral predominantly central interstitial infiltrates with developing dominant left upper lobe consolidation." Respiratory Panel - testing for influenza and RSV - obtained on (b) (6). Results were negative for both RSV and Influenza.

Diagnostic results (unless otherwise stated, normal values were not provided): On (b) (6), Oxygen saturation result was 88 % (normal low: 95, normal high: 100).

Investigator comments:
Subject presented to the after hours pediatric clinic on (b) (6) with a 3 day history of cough and upper respiratory congestion. Patient had a temp of 99.3 F at home on (b) (6) and was given Tylenol by mother. Subject maintained normal oral intake and urine output. His upper respiratory symptoms continued to worsen and mother brought him to after hours clinic. There he had an intial temperature of 102.9 F. Tylenol was given. He had an inital oxygen saturation 88-91%. On examination, he had middle ear erythma and bulging in the right ear. Left tympanic membrane could not be visualized due to cerumen impaction. Decreased air movement on his left side. There were transmitted upper airway sounds, decreased breath sounds on the left side and rhonchi in the left upper, middle and lower lung fields. The remainder of his exam was within normal limits. He was diagnosed with acute otitis media and left upper lobe pneumonia (confirmed with chest x-ray). Due to the low oxygesaturation, subject was placed on supplemental blow by oxygen. Amoxicillin was started for pneumonia and otitis media and a respiratory swab was obtained to look for influenza and RSV both of which were negative. It was decided to admit the subject due to the poor oxygenation status. By the time that he arrived to the inpatient floor he was stable on room air. The plan at this point is to admit him for the night to be sure that

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his oxygenation status remains stable. If not he will have supplemental oxygen provided as needed. Once he has a sustained stable oxygen level on room air he will be discharged.

Study Number: 201234

Study Center ID: 210155

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Accidental exposure to product

Non-Serious Events:

Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6) 20:00, 54 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 accidental ingestion of drug. Serious criteria included hospitalization and life threatening. The subject was treated with naloxone. The outcome of accidental ingestion of drug was recovered/resolved on 11th January 2015 17:56.

The investigator considered that there was no reasonable possibility that the accidental ingestion of drug may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

INVESTIGATOR TEXT

Subject and mother were at a friends home at about 1900 on (b) (6), when mom noticed something yellow in the childs mouth. Mom swept her mouth and found a yellow pill which was believed to be a klonopin 1 mg tablet as the friend was on that medication. Mom reported that about 15 minutes after the child had it in her mouth she began to get lethargic and was walking as if she were drunk. She never lost consciousness but fell to the floor. Mom brought her to the local emergency department. Upon arrival in the ED she was found to have a desaturation down to 88% and shortly after than became apneic and had a desaturation down to the mid 70's. It was also noted that she had pinpoint pupils. Intravenous Narcan 0.2 mg was administered. It was felt that the IV had infiltrated so Narcan 0.4mg was administered right after via IM route. This caused her to awaken and go back almost to baseline with some noted drowsiness. In the ED a urine toxicology screen, urinalysis, aspirin level,
tylenol level, BMP, CBC and EKG were all performed and found to be within normal limits (values not available to site at this time). It was decided to transfer her to a Children's Hospital for further observation to be sure that she had no further respiratory distress in relation to the ingestion. She was admitted to the Children's Hospital on (b) (6) at 0053. Upon arrival and throughout the admission the child's vital sign remained stable. The next morning the child was witnessed walking with normal gait, neurological exam was completely normal, pupils were normal sized. Toxicology medically cleared that patient with an

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exact ingestion still unknown. Of note, mom states that she has liquid methadone at home but it is kept well away from where a child can get to it and mom states she must get a chair to reach it herself. Given the seriousness of this event, Child Protective Services (CPS) were contacted. A CPS worker came to the hospital and met with
the mother. CPS cleared the child for discharge to home with mother. They will continue to follow up. Child was discharged to home in the mothers care on (b) (6) at 1756.

Study Number: 201234

Study Center ID: 210155

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Asthma

Non-Serious Events:

Narrative: This 2-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included asthma.

On (b) (6) 08:00, 120 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 asthma aggravated. Serious criteria included hospitalization. The subject was treated with ipratropium bromide + salbutamol sulfate (Duoneb), methylprednisolone sodium succinate (Solu-Medrol), prednisolone, sodium chloride (Sodium Chloride Solution), prednisolone and fluticasone. The outcome of asthma aggravated was recovered/resolved on 17th April 2015.

The investigator considered that there was no reasonable possibility that the asthma aggravated may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator comments:
Subject started to have a runny nose and cough on 11apr2015. On (b) (6), subject awoke and had shortnes of breath and wheezing. Mom brought him to ED. In the ED he recieved 3 Duonebs, SOlumedrol and IV fluid bolus. He continued to be tachypneic and still had retractions. It was decided to admit him for further observation and management. Once admitted to the hospital, he was started on his normal albuterol regimen form home initially every 2 hours and then every 4 hours. He required no intermittent prn doses of albuterol. He was started on oral prednisolone. At discharge he was started on flovent. He was discharged home with 5 more days of prednisolone. He was no longer tachypneic nor was he retracting at discharge. He was dioscharged to home on (b) (6).

Study Number: 201234

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Study Center ID: 210296

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Respiratory syncytial virus bronchiolitis

Non-Serious Events:

Narrative: This 14-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6) 12:29, 44 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 respiratory syncytial virus bronchiolitis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with amoxicillin, salbutamol (Albuterol), sodium chloride (Normal Saline), lactobacillus nos (Lactobacillus), macrogol (Miralax), paracetamol (Acetaminophen), ibuprofen, nystatin and prednisolone. The outcome of respiratory syncytial virus bronchiolitis was recovered/resolved on (b) (6).

The investigator considered that there was no reasonable possibility that the respiratory syncytial virus bronchiolitis may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: chest x-ray, blood panels, respiratory panel dates were on admission of (b) (6) and continued through out hospitalization ending on (b) (6).

INVESTIGATOR TEXT
seen on (b) (6) for upper respiratory infection and fever. Was seen again in clinic on (b) (6) diagnosed with Bronchiolitis due to respiratory syncytial virus. Was admitted to hospital with mild respiratory distress and dehydration. Treated and discharged on (b) (6)

Study Number: 201234

Study Center ID: 210296

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Dehydration

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Non-Serious Events:

Narrative: This 16-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 72 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 dehydration. Serious criteria included hospitalization. The subject was treated with cefdinir. The outcome of dehydration was recovered/resolved on 1st April 2015.

The investigator considered that there was no reasonable possibility that the dehydration may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Comments:
Admitted on (b) (6) for otitis media, fever, dehydration and diarrhea. Was admitted for rehydration continue on Cefdinir.
Subject was with cold symptoms for 1.5 week taken to clinic 3 days prior to admission and diagnosed with left otitis media. Was started on Cefdinir, got 3 doses so far.
Discharge diagnosis dehydration improved, fever resolved, and Otitis media improving. Discharged on (b) (6)

Study Number: 201234

Study Center ID: 210301

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Groin abscess, Cellulitis

Non-Serious Events:

Narrative: This 12-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

Concurrent medical conditions included pimple.

On (b) (6), less than a day after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 groin abscess. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included severe - grade 3 cellulitis of abdominal wall on (b) (6) with serious criteria of hospitalization and GSK medically significant. The subject was treated with mupirocin (Mupirocin Ointment) and clindamycin. The outcome of groin abscess was recovered/resolved

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on (b) (6) . The outcome(s) of the additional event(s) included cellulitis of abdominal wall (recovered/resolved on 22nd December 2014).

The investigator considered that there was no reasonable possibility that the groin abscess and cellulitis of abdominal wall may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Limited abdomen ultrasound. Impression: Edema within the subcutaenous fatty soft tissues of the lower abdome.

Investigator comments:
Mother noticed a pimple like place on patients groin area about (b) (6) . He was seen by his PCP but was not given any antibiotis. He was started on Mupirocin oint. for ongoing diaper rash/Diaper Dermatitis. Patient then started to run a high fever and the area became warm, tnder and red and was taken to the emergency room and was then admitted to the hospital on (b) (6) for the abscess/cellulitis. Patient was given IV antibioitcs and was then sent home (b) (6) with PO abibiotics. On (b) (6) was in to see PCP for receheck and the abscess had become red, warm and tender.PCP then advisied to readmit the the hospital for further IV antibiotics. and was discharged (b) (6) Subject was treated with Mupirocin Ointment from 02Dec2014-04Dec2014

Study Number: 201234

Study Center ID: 210309

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Croup infectious

Non-Serious Events:

Narrative: This 19-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6) , for prophylaxis.

On (b) (6) , 31 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 croup. Serious criteria included hospitalization and GSK medically significant. The subject was treated with dexamethasone (Decadron), epinephrine (Racemic Epinephrine) and ibuprofen. The outcome of croup was recovering/resolving.

The investigator considered that there was no reasonable possibility that the croup may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: X ray of soft tissue neck (b) (6) . No acute abnormalities. Airway: The subglottic airway is narrowed. The AP dimension of the subglottic airway is 2 mm. This would be compatible with

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localized subglottic inflammatory changes possible from croup. BONES: No acute abnormalities. Other: No other acute abnormalities.

Investigator Comments:
11/21/2014 Mom stated that patient started having a "seal-like" barking. (b) (6) Mom took patient to the emergency department for continued barking cough, where he was given a dose of steroids and instructed to use comfort measures to help with the coughing. i.e. going out in the cold or using humidified air. (b) (6) Mom brought patient to emergency room again for worsening symptoms of barking cough where he received 2 doses of racemic epinephrine and another dose of decadron. Plan was discussed with mom about the best options for care for patient and it was decided to admit him to hospital for night due to worsening symptoms at night and prior 2 emergency room visits. (b) (6) Mom stated that he woke up this am and had an increased work of breathing with multiple retractions. He was given a treatment of racemic epinephrine and patient's breathing improved. He was discharged to home. (b) (6) UPDATE: Unable to obtain stop date for SAE due to lost contact to follow up. Patient dropped on 01/21/2015. 06/04/2015 Will not be getting stop date for Ibuprofen as subject is LOST TO FOLLOW UP.

Study Number: 201234

Study Center ID: 210310

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 21-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received Flu Q-QIV vs Fluzone Quadrivalent on (b) (6), for prophylaxis.

Concurrent medical conditions included otitis media serous. Concomitant products included amoxicillin.

On (b) (6), 168 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The subject was treated with diazepam. The outcome of febrile seizure was recovered/resolved on (b) (6)

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Relevant laboratory workup collected on (b) (6) include the following:
Blood culture: No growth after 12hrs, 24hrs, 48hrs, 3days and 4 days

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CBC: WBC value at 15.5K/uL WNL(range: 6.2-17.0 K/uL), neutrophils at 7.4 WNL (range: 1.9-8.0K/uL), lymphocytes at 6.1 WNL (range: 0.9-5.2K/uL), monocytes at 1.8 high (range: 0.16-1.0K/uL)
EEG completed on (b) (6) WNL

Investigator comments:
As per EDC query resolution, non-serious AE febrile seizure noted on 3/27/15 has been updated to a SAE due to meeting criteria as a potential risks in the Risk Management Plan per protocol. Per PCP visit on (b) (6), subject was diagnosed with Acute Serous Otitis Media to left ear and begin a 10-day antibiotic course of Amoxicillin that same day. On (b) (6) parent admitted subject to nearby emergency room after subject experienced a brief episode of convulsions and continuing high fever. Relevant diagnostic lab workup was completed as well as EEG. Per PCP follow-up on (b) (6), subject has been well since event; no fevers or seizures. Per required HRA SOP follow-up call on (b) (6), parent reports subject still doing well with no AE's, particularly of fever and seizure since last study contact on 3/27/15.

Study Number: 201234

Study Center ID: 210310

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Multiple injuries

Non-Serious Events:

Narrative: This 22-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 82 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 multiple injuries. Serious criteria included hospitalization. The subject was treated with paracetamol (Infant Tylenol) and ibuprofen. The outcome of multiple injuries was recovered/resolved on 22nd February 2015.

The investigator considered that there was no reasonable possibility that the multiple injuries may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: X-ray of left arm confirm no fractures per PCP/PI.

Investigator Text:
PCP/PI of subject called research site on 2/4/15 to disclose the following event. On (b) (6), subject was playing behind grandmother's car and was aaccidentally hit when car backed up. According to hospital records, subject suffered mild abrasions to right face, left arm, left chest and abdomen and left thigh; no immediate treatment needed. However, lacerations were found on subject's left hand which were repaired

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with dissolvable suture. Orthopedics was consulted to monitor patient's left arm, x-rays obtained confirm no fractures. Subject was placed initially in pediatric intensive care for observation, but later transferred to the medical floors and discharged home the following day. Total hospitalization course two days; (b) (6) . On (b) (6), subject was seen by PCP as follow-up from hospitalization. PCP/PI note subject has no limitations to movement of his arm and is improving without complications.

Study Number: 201234

Study Center ID: 210317

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Pneumonia

Non-Serious Events:

Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6) , for prophylaxis.

On (b) (6) , 161 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 pneumonia. Serious criteria included hospitalization and GSK medically significant. The outcome of pneumonia was recovered/resolved on 20th March 2015.

The investigator considered that there was no reasonable possibility that the pneumonia may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator comments:
Subject's LAR reported that subject was diagnosed with Pneumonia in the left lung and was hospitalized from (b) (6) . Records are pending.
New medical release form was sent to LAR, which has not been sent back. LAR has not responded to left messages. Medical records have not been received therefore concomitant medications and diagnostic testing during hospital stay are unknown. Also due to no LAR response, we are not able to confirm start and stop dates of symptoms prior to and after hospitalization.

Study Number: 201234

Study Center ID: 210320

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

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Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Staphylococcal abscess

Non-Serious Events:

Narrative: This 13-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 2 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 staphylococcus aureus abscess. Serious criteria included hospitalization and GSK medically significant. The subject was treated with mupirocin (Bactroban), sulfamethoxazole, trimethoprim (Septra), clindamycin, midazolam (Versed) and clindamycin. The outcome of staphylococcus aureus abscess was recovered/resolved on 9th December 2014.

The investigator considered that there was no reasonable possibility that the staphylococcus aureus abscess may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Wound Culture positive for Staphylococcus Aureus

INVESTIGATOR TEXT
patient presented to PCP office on (b) (6) with abscess on right posterior medial thigh and was diagnosed with Cellulitis and abscess and was given prescriptions of Bactroban and Septra. Due to worsening of abscess patient went to local hospital ER on (b) (6). From local hospital she was then transferred to another hospital for surgery on abscess. Incision and draingage was performed on (b) (6). Patient was discharged on (b) (6) to home. Patient followed up with PCP on (b) (6) and abscess was resolved, however subject continued to take medicine for this until 12/9/14.

Study Number: 201234

Study Center ID: 210320

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Dehydration

Non-Serious Events:

Narrative: This 11-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

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Concurrent medical conditions included diarrhea.

On (b) (6), 115 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 dehydration. Serious criteria included hospitalization. The subject was treated with potassium chloride + sodium chloride and sodium chloride. The outcome of dehydration was recovered/resolved on 5th May 2015.

The investigator considered that there was no reasonable possibility that the dehydration may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: stool culture collected on (b) (6) showed no salmonella, shigella, campylobacter or staph aureus isolated. yeast noted.

INVESTIGATOR TEXT
subject presented to clinic on (b) (6) with fever and vomiting. Mother then reported via phone call on 5/1/15 that subject had diarrhea, mother was instructed to bring child to clinic or ER if not any better. Diarrhea continued therefor parent brought subject to to ER on (b) (6) and was admitted for dehydration. subject was discharged from hospital on (b) (6).

Study Number: 201234

Study Center ID: 210329

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Seizure

Non-Serious Events:

Narrative: This 19-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included family history of seizure.

On (b) (6), 103 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 seizure. Serious criteria included hospitalization and GSK medically significant. The outcome of seizure was recovered/resolved on 18th March 2015.

The investigator considered that there was no reasonable possibility that the seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

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Relevant Tests: (b) (6) BUN/CREATININE RATIO 75.0 H (NL=7.0-25.0)
(b) (6) EEG abnormal,
Head CT negative,
MRI Brain resullts are normal for age Diagnostic results (unless otherwise stated, normal values were not provided):
On (b) (6), Blood urea result was 15 mg/dL (normal low: 0.7, normal high: 1.2), Haematocrit result was 35.3 % (normal low: 36, normal high: 51), Mean cell volume result was 82.4 fL (normal low: 90, normal high: 112), Mean platelet volume result was 7.0 fL (normal low: 7.4, normal high: 10.4) and Monocyte count result was 8.7 % (normal low: 0.00, normal high: 7).

INVESTIGATOR TEXT
Parents took subject to ER on (b) (6) at 18:01 with reported episodes where here muscles with stiffen and she will shake some. She stares off during the episodes. After, she willl respond, but not during. The episodes occur several times daily. The onset of the presenting problems starteed 1 week ago. Subject was admitted on (b) (6) with a primary diagnosis of Seizure. Condition was reported as stable. Subject was discharged on (b) (6). -

Study Number: 201234

Study Center ID: 210639

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Kawasaki's disease, Urinary tract infection

Non-Serious Events:

Narrative: This 17-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 93 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed not applicable kawasaki's disease. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included moderate - grade 2 urinary tract infection on (b) (6) with serious criteria of hospitalization. The subject was treated with acetylsalicylic acid (Aspirin), immunoglobulin human normal (Immune Gamma Globulin) and ceftriaxone. The outcome of kawasaki's disease was recovering/resolving. The outcome(s) of the additional event(s) included urinary tract infection (recovered/resolved on 3rd February 2015).

The investigator considered that there was no reasonable possibility that the kawasaki's disease and urinary tract infection may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: ALT 630U/L AST 696U/L , cath urinalysis, cath urine culture on (b) (6) Diagnostic

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results (unless otherwise stated, normal values were not provided): On (b) (6), Alanine aminotransferase result was 630 u/L (normal low: 9, normal high: 52), Aspartate aminotransferase result was 696 u/L (normal low: 14, normal high: 42), Blood albumin result was 4.0 (normal low: 3.5, normal high: 5), Blood alkaline phosphatase result was 389 u/L (normal low: 9, normal high: 52), Blood bicarbonate result was 21 mEq/L (normal low: 23, normal high: 34), Blood calcium result was 10.6 mg/dL (normal low: 8.5, normal high: 10.4), Blood chloride result was 102 mEq/L (normal low: 98, normal high: 107), Blood creatine result was 0.3 mg/dL (normal low: 0.8, normal high: 1.3), Blood glucose result was 100 mg/dL (normal low: 70, normal high: 99), Blood potassium result was 4.4 mEq/L (normal low: 3.5, normal high: 5.1), Blood sodium result was 137 mEq/L (normal low: 136, normal high: 145), Blood urea result was 22 mg/dL (normal low: 7, normal high: 18), Haematocrit result was 39.4 % (normal low: 38, normal high: 47), Haemoglobin result was 12.3 (normal low: 12, normal high: 16), Lymphocyte count result was 47 % (normal low: 35, normal high: 74), Neutrophil count result was 41 % (normal low: 40, normal high: 80), Platelet count result was 343 K/MM3 (normal low: 150, normal high: 375), Red blood cell sedimentation rate result was 51 mm/hr (normal low: 0.00, normal high: 20) and White blood cell count result was 10.3 K/MM3 (normal low: 4.3, normal high: 11).

INVESTIGATOR TEXT:
17 mo old female who on 1/18 had onset of leg rash; on 1/19 and 1/20 with fever and continued rash but playful; on 1/21 with more diffuse rash, cont fever but now more irritable, not as playful. On (b) (6) seen in ER for temp, fussiness, no blood/urine collected but quick strep was negative, throat cx also collected. On (b) (6) seen by P.I. with cont fever, rash, and red eyes without d/c; presented also with strawberry tongue, pharynx injected without exudate, lips red but not cracked; patient had mild shoddy bilat cervical nodes present. Heart lungs abd all negative, skin with diffuse, red macular confluent blanching rash noted but no peeling of skin appreciated. Gait normal, CBC,ESR,CMP, Blood cultures done on (b) (6). Seen (b) (6) for follow up with continued symptoms, more irritable, more febrile as parents were directed not to dose with antipyretics. Was admitted for evaluation and underwent heart echo, repeat blood tests cath urine analysis, throat culture. Diagnosed with UTI and Kawasaki's disease and treated with IV immune globulin, high doses of asprin and IV antibiotics. Discharged on (b) (6) LABS DATED: (b) (6) CBC: WBC 10.3, hemoglobin 12.3, hematocrit, 39.4, platelets 343, with 41%neutrophils and 47% lymphocytes. ESR: 51 CMP: Glucose 100, sodium 137, potassium 4.4, chloride 102, bicarbonate 21, BUN 22, creatinine 0.3, calcium 10.6, albumin 4.0, AST 696, ALT 630, alkaline phosphatase 389 BLOOD CULTURE RESULTS: no growth after 5 days.

This case contains an event (Kawasaki Disease) assessed by the investigator as a serious possible immune mediated disorder (pIMD).

Study Number: 201234

Study Center ID: 210664

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Gastroenteritis, Dehydration, Hyponatraemia

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Non-Serious Events:

Narrative: This 2-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 83 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 acute gastroenteritis. Serious criteria included hospitalization. Additional event(s) included moderate - grade 2 dehydration on (b) (6) with serious criteria of hospitalization and moderate - grade 2 hyponatremia on (b) (6) with serious criteria of hospitalization. The subject was treated with ondansetron (Zofran (Ondansetron)), glucose (Dextrose), sodium chloride, d5ns + kcl solution and dextrose + half normal saline. The outcome of acute gastroenteritis was recovered/resolved on 8th January 2015. The outcome(s) of the additional event(s) included dehydration (recovered/resolved on 8th January 2015) and hyponatremia (recovered/resolved on 8th January 2015).

The investigator considered that there was no reasonable possibility that the acute gastroenteritis, dehydration and hyponatremia may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Urine Mircoscopic Test-Glucose 500 mg/dL(Normal Range-NEG), Ketones 100 mg/dL (Normal Range-NEG) Chest XRay-Negative (Normal Range-Normal/Negative) Diagnostic results (unless otherwise stated, normal values were not provided): On 7th January 2015, Blood chloride result was 100 mmol/L (normal low: 101, normal high: 111), Blood sodium result was 129 mmol/L (normal low: 134, normal high: 146), Blood urea result was 31.9 ratio (normal low: 5, normal high: 18) and Carbon dioxide result was 15 mmol/L (normal low: 20, normal high: 35).

Investigator comments:
Patient went to the ED w/ Mother on (b) (6) for evaluation of vomiting, diarrhea and fever. Temp was 99.7 at ED. Per parent, began w/ vomiting on 1/5/2015. Diarrhea began on 1/6/2015. At ED visit, given oral anti-nausea medication x once. Oral rehydration was tolerated therefore the patient was discharged with a Vomiting/Diarrhea - "Likely Viral" Diagnosis. Rx given for nausea/vomiting for home use. On (b) (6), the patient returned to the ED for continuous vomiting and decreased appetite, plus diarrhea. At this visit, the patient was admitted to the hospital with a diagnosis of Acute Gastroenteritis and Hyponatremia. The patient was given IV therapy for rehydration overnight due to low sodium levels along with oral anti-nausea medication (Dextrose 5% w/ 0.45% NaCL 1,000 mL and Ondansetron Tablet). By the next day, (b) (6), the patient had not vomited or had diarrhea. IV fluids were discontinued at discharge. Repeat labs were done. CO2 was 20 mmol/L and Na was 136+ - which both were within normal ranges. At discharge on (b) (6), the patient had good improvement and oral foods were tolerated.

Study Number: 201234

Study Center ID: 210664

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID (b) (6)

Confidential
Unblinded Report – With Suspect Products and Serious and Non-Serious Events

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Bronchiolitis

Non-Serious Events:

Narrative: This 12-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 1 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 bronchiolitis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with salbutamol (Albuterol), salbutamol (Albuterol), ipratropium bromide (Atrovent), ibuprofen (Motrin), prednisolone sodium phosphate (Orapred), paracetamol (Tylenol), lidocaine + tetracaine (Synera Patch) and sodium chloride (Normal Saline). The outcome of bronchiolitis was recovered/resolved on 22nd December 2014.

The investigator considered that there was no reasonable possibility that the bronchiolitis may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: RSV Screen (b) (6) - negative Influenza A/B and AH1N1 Amplified process-negative Chest Xray - Lung parenchyma is clear of focal airspace opacity. There is peribronchial cuffing and perihilar atelectasis. There is hyperinflation. There is no pleural effusion and no pneumothorax. There is left sided aortic arch. The airway is patent. Impression: Viral or reactive small airways disease. No focal pneumonia.

Investigator Text:
Patient presents to ED (b) (6) - has been sick x 3 days with congestion, fever and shortness of breath. Patient with upper airway congestion and tachypnea. 12 month old with past medical history of wheezing. Mom states that she has given him some albuterol but that he is still breathing hard and wheezing. He has had a fever. After several examinations patient remains very tachypneic with retractions. His RSV is negative, his chest xray is negative. Admission is needed. Admitted on (b) (6). Diagnosis is bronchiolitis.
Patient was discharged on (b) (6) on Albuterol via nebulizer and to follow up with his PCP with the next few days.

Study Number: 201234

Study Center ID: 210666

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Abscess, Cellulitis

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Non-Serious Events:

Narrative: This 12-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. On (b) (6), the subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) for prophylaxis.

On (b) (6), 5 days after receiving Flu Q-QIV vs Fluzone Quadrivalent the subject developed severe - grade 3 right thigh cellulitis. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included severe - grade 3 left thigh cellulitis on (b) (6) with serious criteria of hospitalization and GSK medically significant and severe - grade 3 multiple abscesses on (b) (6) with serious criteria of hospitalization. The subject was treated with sulfamethoxazole, trimethoprim (Septra), fentanyl, clindamycin and ibuprofen. (Dechallenge was positive). The outcome of right thigh cellulitis was recovered/resolved on 18th November 2014. The outcome(s) of the additional event(s) included multiple abscesses (recovered/resolved on 18th November 2014) and left thigh cellulitis (recovered/resolved on 18th November 2014).

The investigator considered the right thigh cellulitis, right thigh cellulitis, right thigh cellulitis, right thigh cellulitis, left thigh cellulitis, left thigh cellulitis, left thigh cellulitis, left thigh cellulitis, left thigh cellulitis, multiple abscesses, multiple abscesses, multiple abscesses and multiple abscesses to be not reported if related to Flu Q-QIV vs Fluzone Quadrivalent. The investigator considered that there was no reasonable possibility that the right thigh cellulitis, left thigh cellulitis and multiple abscesses may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Ultrasound of leg - (b) (6) - no fluid collection
Wound culture - (b) (6) - MRSA

Diagnostic results (unless otherwise stated, normal values were not provided).

Investigator comments : (b) (6) - Patient presented to office for hospital follow up today. She is a 13 month old who had a forearm abscess the month prior to study enrollment and a household contact with an even more recent abscess. She presented to the office with a draining left thigh abscess and bilateral thigh cellulitis on (b) (6). She was started on oral Septra and instructed to return if symptoms worsened, She became febrile and was seen at a local emergency room on (b) (6). She had an elevated white count but an ultrasound was negative for fluid collections. She was started on IV Clindamycin and transferred to the MUSC Children's Hospital. She was admitted from the ER there. Multiple abscesses were drained surgically on (b) (6). She was switched to oral Clindamycin for discharge based on wound culture sensitivities. All symptoms were improved at visit today.
(b) (6) - Skin examined at Visit 2 with no residual findings except 3 well healed surgical scars.

Study Number: 201234

Study Center ID: 210670

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Confidential
Unblinded Report – With Suspect Products and Serious and Non-Serious Events

Suspect Products: Fluzone Quadrivalent

Serious Events: Hemiplegia, Developmental delay

Non-Serious Events:

Narrative: This 3-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

Concurrent medical conditions included cerebral palsy.

On (b) (6), 76 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 hemiplegia. Serious criteria included disability and GSK medically significant. Additional event(s) included moderate - grade 2 developmental delay on 16th February 2015 with serious criteria of disability. The outcome of hemiplegia was not recovered/not resolved. The outcome(s) of the additional event(s) included developmental delay (not recovered/not resolved).

The investigator considered that there was no reasonable possibility that the hemiplegia and developmental delay may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Text:
3 year old male presented for well child check on (b) (6) mother expressed concerned of a few odd movements. Child has always run/walked holding his L arm flexed rather than swinging naturally as his other arm does. Also, walks on toes more to R foot than L and gait is unsteady - mom feels he falls more than he should. Positive family history of member with Cerebal Palsey. Developmentally met milestones in first year of life. Referred to Special Services with right hemiplegia as characterized by increased muscle tone in right side of body, Upper Extrimity/Lower Extrimity asymmetries noted in that right Upper Extrimity flexes up with fisted hand with increased velocity/effort with activity with poor Bilateral Upper Extrimity midline cross and decreased quality of performance in Bilateral Upper Extrimity activities. He demonstrates mild delay in developmental skills with most at the 2 - 21/2 year level.
Child would benefit form outpatient Occupational Therapy to assist in facilitating improved overall alignment and symmetry, improved Bilateral Upper Extrimity function for optimal participation and performance in play/learning activities and self care tasks. Goals as follows: In 12 weeks: 1. incorporate Right Upper Extrimity into bilateral activity with no more than 1 verbal cue 3/5x. 2. use both hands to unbutton 3 buttons with min assist3/5x. 3. use both hands to catch a medium sized ball 3/5x. 4. demonstrate right radial digital grasp of cube 50% of time. 5. demonstrate right pincer grasp of small object 50% of time. 6. push Bilateral Upper Extrimities through sleeves to don a shirt independently 3/5x. 7. Family will be independent in HEP. Potential for achieving developmental milestones: good with therapy.
Subject has completed 3 physical therapy appointments as is doing well though he does know when tasks asked of him are difficult and needs encouragement to try. Subject has completed 2 occupational therapy appointments, the first session states that the subject had good participation but cries when challenged and is easily redirected.

Study Number: 201234

Study Center ID: 210671

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Unblinded Report – With Suspect Products and Serious and Non-Serious Events

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Dehydration, Gastroenteritis

Non-Serious Events:

Narrative: This 21-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 112 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 dehydration. Serious criteria included hospitalization. Additional event(s) included severe - grade 3 gastroenteritis on (b) (6) with serious criteria of hospitalization. The outcome of dehydration was recovered/resolved on 11th February 2015. The outcome(s) of the additional event(s) included gastroenteritis (recovered/resolved on 11th February 2015).

The investigator considered that there was no reasonable possibility that the dehydration and gastroenteritis may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

INVESTIGATOR TEXT
Subject came in to office on (b) (6). Severe dehyrdration. Hospital admission for IV hydration - (b) (6). Subject came into our office with the chief complaint being vomiting, loose stools, decreased appetite and decreased fluid intake since (b) (6). Subject initially admitted to hospital for 24 hour observation. However, subject did not tolerate PO intake and remained in the hospital for another day. During subjects stay in hospital he remained afebrile, vital signs were stable, had much improved urine output. Prior to discharge subject was eating well, no vomiting, and only one BM. Final diagnosis was Dehydration with Gastroenteritis.

Study Number: 201234

Study Center ID: 210671

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Dehydration

Non-Serious Events:

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Unblinded Report – With Suspect Products and Serious and Non-Serious Events

Narrative: This 17-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 126 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 dehydration. Serious criteria included hospitalization. The outcome of dehydration was recovered/resolved on 28th February 2015.

The investigator considered that there was no reasonable possibility that the dehydration may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

On 01jul2015, the investigator updated the relationship to NO. Per the Principle Investigator's review there is no reasonable possibility that this episode of Dehydration was related to the investigational product. The answer has been changed to "NO" per investigator. This was an oversight.

Investigator Text:
Dehydration. Hospital Admission (b) (6). Discharged (b) (6). Subject came into office for vomiting and diarrhea on (b) (6). Subject was admitted to hospital on (b) (6) with dehyrdration secondary to vomiting and diarrhea. No fever, no cough. After IV rehydration, subject started to improve. Voiding well, drinking well. Still had diarrhea with decreased frequency. Subject was stable enough to be discharged on (b) (6) to continue recovery of diarrhea at home. However, dehydration resolved on 2/28/15.

Study Number: 201234

Study Center ID: 210672

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Gastroenteritis rotavirus

Non-Serious Events:

Narrative: This 3-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 111 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 rotavirus gastroenteritis. Serious criteria included hospitalization and GSK medically significant. The subject was treated with ondansetron (Zofran), lactobacillus acidophilus, lactobacillus bulgaricus (Lactinex), hyoscyamine sulfate (Levsin) and normal saline + potassium chloride. The outcome of rotavirus gastroenteritis was recovered/resolved on 7th March 2015.

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Unblinded Report – With Suspect Products and Serious and Non-Serious Events

The investigator considered that there was no reasonable possibility that the rotavirus gastroenteritis may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Rotavirus test was positive on (b) (6) Diagnostic results (unless otherwise stated, normal values were not provided): On (b) (6) , Blood sodium result was 129 mmol (normal low: 136, normal high: 145), Blood urea result was 17 mg (normal low: 2, normal high: 18), Oxygen saturation result was 14 mg (normal low: 7, normal high: 18) and White blood cell count result was 19.60 unknown (normal low: 4.5, normal high: 14.9).

Investigator Comments:
Child was in doctor's office on (b) (6) and was diagnosed with Gastroenteritis. Child returned to office on (b) (6) feeling worse and after lab test was determined to be dehydrated with Gastroenteritis and was admitted to hospital. On (b) (6) child was discharged from the hospital and Gastroenteritis and dehydration was resolved. Vital were normal, child was playful and happy.

Study Number: 201234

Study Center ID: 210672

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Gastroenteritis

Non-Serious Events:

Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6) , for prophylaxis.

On (b) (6) , 79 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 gastroenteritis. Serious criteria included hospitalization. The subject was treated with ondansetron (Zofran) and d5w + 1/2 normal saline. The outcome of gastroenteritis was recovered/resolved on 12th February 2015.

The investigator considered that there was no reasonable possibility that the gastroenteritis may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Comment:
Patient came to pediatricians office on (b) (6) with vomiting and diarrhea. Diarrhea began on 2-6-15, while vomiting began on 02-08-15. Patient had decreased urinary output. While in office patient was found to be dehydrated and was admitted to hospital for gastroenteritis. Subject was admitted into hospital on (b) (6) and discharged on (b) (6)

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Study Number: 201234

Study Center ID: 210816

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 14-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 39 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The subject was treated with paracetamol (Tylenol) and ibuprofen. The outcome of febrile seizure was recovered/resolved on (b) (6).

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

INVESTIGATOR TEXT
Patient and family were traveling during time of SAE. Patient began with congestion with no fever on December 24, 2014. Patient developed fever on morning of (b) (6). Patient had fever of 103 degrees the evening of (b) (6), resulting in febrile seizure. Parents called ambulance. Patient transported to ER. Patient was given ibuprofen, examined and monitored. Patient was also given tylenol earlier on (b) (6). Once fever reduced, patient was discharged from ER. There was no follow-up appointment after the patients' ER visit. Patient had a normal well check on (b) (6) and has had no other febrile seizures since this event.

Study Number: 201234

Study Center ID: 210865

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Craniocerebral injury, Concussion

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Unblinded Report – With Suspect Products and Serious and Non-Serious Events

Non-Serious Events:

Narrative: This 2-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6) 18:08, 88 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 closed head injury. Serious criteria included hospitalization and GSK medically significant. Additional event(s) included moderate - grade 2 concussion on (b) (6) 18:08 with serious criteria of hospitalization. The subject was treated with fentanyl and ondansetron (Zofran). The outcome of closed head injury was recovered/resolved on 29th January 2015. The outcome(s) of the additional event(s) included concussion (recovered/resolved on 29th January 2015).

The investigator considered that there was no reasonable possibility that the closed head injury and concussion may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: (b) (6) - CT Scan, Head Without Contrast: No acute intracranial abnormalities identified.

INVESTIGATOR TEXT

On (b) (6) subject fell approximately four feet, backwards out of a shopping cart. He hit the back of his head on a tile floor. Mother of subject reports brief loss of consciousness after crying immediately post fall. Per parents, child seemed "urpy" and "pale" and "irritable", so they took him to a local Emergency Room. He was treated there for a closed head injury. A CT scan was performed to rule out intracranial bleed. Two doses of Fentanyl were given, intranasal, prior to the CT scan. The CT results were as follows, no acute intracerebral CT abnormalities identified. One dose of ODT Zofran was also given to decrease vomiting. The subject was discharged home the same day, (b) (6), subject was seen in follow up by his primary care physician. Symptoms of concussion, due to closed head injury, continue to improve. No further medications given. There are no relevant risk factors noted. Possible cause of the event is accidental fall, resulting in closed head injury and concussion. On (b) (6), subject returned to clinic to follow up. Diagnosis head concussion. Symptoms continue to improve. Light and sound aversion have improved. Appetite still decreased, but weight is stable, and appetite increasing over the past week. No further concerns noted. Head concussion, resolved.

Study Number: 201234

Study Center ID: 210865

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Sexual abuse

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Unblinded Report – With Suspect Products and Serious and Non-Serious Events

Non-Serious Events:

Narrative: This 3-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 66 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed mild - grade 1 sexual assault. Serious criteria included hospitalization. The outcome of sexual assault was recovered/resolved on (b) (6) 19:22.

The investigator considered that there was no reasonable possibility that the sexual assault may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Text:
On (b) (6) subject was seen at a local Emergency Room due to an alleged sexual assault that occurred five days prior on (b) (6). Physical exam found to be normal per Emergency Room report. The alleged sexual assault was reported to the proper agencies. Subject was discharged home the same day, (b) (6). There were no medications given. No diagnostic tests were performed. No pertinent family or social history noted. Parent (s) instructed to follow up with provider and a center for sexual assault. Additional information will be provided if it becomes available.
Subject was seen on (b) (6). Mother reported that the alleged sexual assault was investigated. She states she has no other concerns regarding this issue and she does not believe subject was actually assaulted.

Study Number: 201234

Study Center ID: 210867

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Intussusception

Non-Serious Events:

Narrative: This 10-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 7 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 intussusception. Serious criteria included hospitalization and GSK medically significant. The subject was treated with paracetamol (Tylenol). The outcome of intussusception was recovered/resolved on 14th November 2014.

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The investigator considered that there was no reasonable possibility that the intussusception may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

INVESTIGATOR TEXT
patient seen (b) (6) in our office for abdominal pain- then admitted to hospital for evaluation of abdominal pain. ultrasound revealed intussusception. intussusception successfully reduced by radiology using an air enema. monitored overnight and then discharged the next day patient received air enema on (b) (6) only

Study Number: 201234

Study Center ID: 211189

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Asthma

Non-Serious Events:

Narrative: This 18-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 126 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 asthma aggravated. Serious criteria included hospitalization. The outcome of asthma aggravated was recovered/resolved on 24th April 2015 12:00.

The investigator considered that there was no reasonable possibility that the asthma aggravated may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Text:
On 4/22/15, patient's caregiver heard wheezing along with his stomach moving afast and heavy. This event was a result of this condition, causing him to be admitted to the hospiatl on (b) (6). He was discharged on (b) (6).

Study Number: 201234

Study Center ID: 211189

Subject ID: (b) (6)

Randomization Number: UNKNOWN

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Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 16-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6) 13:00, 80 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 simple febrile convulsion. Serious criteria included hospitalization and GSK medically significant. The subject was treated with paracetamol (Acetaminophen). The outcome of simple febrile convulsion was recovered/resolved on 15th February 2015 02:04.

The investigator considered that there was no reasonable possibility that the simple febrile convulsion may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: EKG results: NSR, normal intervals, normal morphology, normal QTc. POC glucose- 73. Both tests performed (b) (6).

Investigator comments:
Patient's mother called Nemours nurse at 3:24 on (b) (6) complaining of a suspected seizure epsiode. Paramedic was called, informed mother that he had a seizure due to fever (and being tightly bundled up). The family was advised to take him to the Emergency Department where he was closely monitored. The total course of hospitalizatoni was (b) (6). SAE unrelated to study product. No other medication was taken by the patient. Family was provided with diastat but did not give any of the med to him.

Study Number: 201234

Study Center ID: 211558

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone

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Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 74 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed mild - grade 1 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The subject was treated with ibuprofen. The outcome of febrile seizure was recovered/resolved on (b) (6).

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator text:
The subject presented on (b) (6) generalized tonic-clonic seizure with eye retroversion; event duration unknown. She was taken to emergency service at Pediatric Hospital where she was found neurologically intact but febrile; she stayed in such setting unknown time under clinical observation and was sent home with oral ibuprofen. She has never received antiepileptic treatment.

Study Number: 201234

Study Center ID: 211558

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Calculus urinary, Urinary tract infection

Non-Serious Events:

Narrative: This 15-month-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 2nd dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 29 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 urolithiasis. Serious criteria included hospitalization. Additional event(s) included moderate - grade 2 urinary tract infection on (b) (6) with serious criteria of hospitalization. The subject was treated with meropenem, ertapenem, furosemide, vecuronium, midazolam, salbutamol, fluticasone propionate (Flixotide), buprenorphine, hydrochlorothiazide, epinephrine (Adrenaline), phytomenadione (Vitamin K), omeprazole, dexamethasone (Dexametasone), amoxicillin (Amoxycillin), fluconazole, paracetamol, cefuroxime and aminophylline. The outcome of urolithiasis was recovered/resolved on 8th April 2015. The outcome(s) of the additional event(s) included urinary tract infection (recovered/resolved on 1st April 2015).

The investigator considered that there was no reasonable possibility that the urolithiasis and urinary tract infection may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

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Relevant Tests: Abdominal ultrasound (b) (6) which showed right hydronephrosis and renal and ureteral lithiasis as well.
Abdominal radiography (b) (6) which showed right renal calcification. Abdominal computarized tomography (b) (6) which showed right renal and ureteral litiasis. On (b) (6) the urine test was reported with yeast so urine culture was performed which was reported on (b) (6) with 50,000colonies of blastoconidias.
Diagnostic results (unless otherwise stated, normal values were not provided): On (b) (6), Alanine aminotransferase result was 43.00 UI/L (normal low: 10, normal high: 34), Aspartate aminotransferase result was 84.00 UI/L (normal low: 10, normal high: 34), Band neutrophil count result was 15 unknown (normal low: 1, normal high: 2), Blood alkaline phosphatase result was 101 UI/L (normal low: 44, normal high: 147), Blood lactate dehydrogenase result was 391.00 UI/L (normal low: 105, normal high: 333), Blood potassium result was 3.90 mEq/L (normal low: 3.5, normal high: 5.0), Haematocrit result was 11.5 g/L (normal low: 10, normal high: 12), Haematocrit result was 35.9 percent (normal low: 33, normal high: 36), Neutrophil count result was 83 % (normal low: 2600, normal high: 5200), Platelet count result was 407000.00 unknown (normal low: 150000, normal high: 400000), Thrombin time result was 38.30 seconds (normal low: 24, normal high: 32) and White blood cell count result was 40,200 unknown (normal low: 5000, normal high: 10000). On (b) (6), pH urine result was 7.0 unknown (normal low: 5.5, normal high: 6.5).

Investigator Text:
Presented the first symptoms on 04/Feb/2015 which were vomiting and irritability; on (b) (6) the subject was taken to the vaccination center where she was diagnosed as pharyngitis, Dimacol was prescribed which was not administered by the mother. On (b) (6) presented vomitin (3), bloating, abdominal pain and absence of bowel movement for 3 days so she was brought to emergency service at pediatric hospital where bowel obstruction versus appendicitis was suspected; abdominal ultrasound was performed on (b) (6) and reported with right hydronephrosis. On (b) (6) abdominal ultrasound so as abdominal radiography were performed and right renal so as ureteral lithiasis were suspected. On (b) (6) abdominal computarized tomography was performed which showed right renal and ureteral lithiasis . The subject stayed hospitalized at emergency room until (b) (6) and moved to the Urology service on (b) (6) date when cistoscopy an double lumen catheter placement was performed.
On (b) (6) were performed cystoscopy, pyelolithotomy and placement of right doublé lumen catheter as well. Current clinical condition of the subject are satisfactory. . On (b) (6) urine test was reported with yeast so urine culture was taken and starts with antifungal therapy . The urine culture reported on (b) (6) showed 50,000 colonies of blastoconidias. On (b) (6) renal ulttrasound was performed which was reported as normal and ruled out the presence of fungomas as well. To date, has not been demonstrated by urine culture planting the fungus causing urinary tract infection. On (b) (6) the dual lumen catheter was withdrawn; the clinical conditions of the subject are satisfactory and has not been identification of the causative fungus by direct seeding of the culture plate. Due to the good clinical evolution of the subject, she was discharged on (b) (6) fully recovered from the serious adverse event without medication.

Study Number: 201234

Study Center ID: 211558

Subject ID: (b) (6)

Randomization Number: UNKNOWN

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Case ID: (b) (6)

Suspect Products: Fluzone Quadrivalent

Serious Events: Otitis media acute, Pharyngitis, Bronchiolitis

Non-Serious Events:

Narrative: This 2-year-old female subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 22 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 pharyngitis. Serious criteria included hospitalization. Additional event(s) included moderate - grade 2 otitis media acute on (b) (6) with serious criteria of hospitalization and moderate - grade 2 bronchiolitis on (b) (6) with serious criteria of hospitalization and GSK medically significant. The subject was treated with metamizole sodium (Metamizol), erythromycin, paracetamol, ambroxol, amoxicillin + clavulanic acid (Amoxycillin + Clavulanic Acid), chloramphenicol, ipratropium bromide + salbutamol and beclometasone. The outcome of pharyngitis was recovered/resolved on 15th January 2015. The outcome(s) of the additional event(s) included bronchiolitis (recovered/resolved on 8th January 2015) and otitis media acute (recovered/resolved on 14th January 2015).

The investigator considered that there was no reasonable possibility that the pharyngitis, otitis media acute and bronchiolitis may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Thorax X ray which showed lung overdystension with no inflitration nor consolidation Blood oxygen saturation 89%
On (b) (6) Platelet count result was 190000.00 cells (normal low: 100000, normal high: 400000) and White blood cell count result was 5200.00 cells (normal low: 5000, normal high: 10000).
Diagnostic results (unless otherwise stated, normal values were not provided): On (b) (6) Haematocrit result was 38.8 % (normal low: 36, normal high: 45), Haemoglobin result was 12.6 g/dL (normal low: 12, normal high: 15), Lymphocyte count result was 52.5 % (normal low: 40, normal high: 60) and Neutrophil count result was 32.0 % (normal low: 30, normal high: 75).

Investigator Text:
Via telephone the father of the subject reported that the child was hospitalized with diagnosis of otitis media in social security hospital on (b) (6); also refers that the subject began with fever and cough on 01/Jan/2015. The treatmen is unknown as well as laboratory an imaging test done. We will follow the adverse event as well as the corresponding reports.
On (b) (6) the subject was taken to the Vaccination Center where the parents mentioned the following: the subject presented the first symtomps on 01/Jan/2015 which were cough and fever on (b) (6) and was taken to the Social Security Clinic where she was diagnosed as pharyngitis and started treatment with Paracetamol, Ibuprofen and erythromicin; because persistence of the symptoms on (b) (6) was taken again to the clinic above mentioned where she was found with respiratory failure, and fever (39°C) which caused her hospitalisation as Bronchiolitis, pharyngitis and acute otitis and started treatment with Amoxicilin, Beclometasone, Combivent and oftalmic cloramphenicol. The subject presented satisfactory clinical evolution and discharged as recovered from Bronchiolitis and recovering of pharyngitis and acute otitis on (b) (6)

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On 16/Jan/2015 telephone contact was made with the mother of the subject who mentioned that became asymptomatic and concluded treatment on 15/Jan/2015; until after the last vaccination on 14/Jan/2015 the subject has not had reactions to it. It is considered fully solved the Serios Adverse Event without sequelae.

Study Number: 201234

Study Center ID: 212890

Subject ID (b) (6)

Randomization Number: UNKNOWN

Case ID (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 19-month-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

The subject's past medical history included fever.

On (b) (6), 50 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed moderate - grade 2 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The subject was treated with ibuprofen (Ibuprofen Oral Suspension). The outcome of febrile seizure was recovered/resolved on (b) (6).

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Relevant Tests: Finger stick blood glucose: 102 Normal range: 100-200.

INVESTIGATOR TEXT
Subject presented to Emergency Department after a febrile seizure at home. Subject picked up from day care, prior to febrile seizure, appearing sleepy. Parent noted subject began to feel warm to the touch and had flushed cheeks. Parent gave one dose of Tylenol. Actual dose unknown. A few minutes later subject began having seizure like activity. No other ill symptoms to report. Emergency medical services took temperature upon arrival and documented 103F. Emergency medical services removed clothing and applied cold towels to subject. Temperature decreased to 99F prior to Emergency Department arrival. Temperature in Emergency Department 101.8F rectally. Subject given one dose of ibuprofen. Temperature decreased to 99.7F rectally. Subject discharged home with diagnosis of febrile seizure. Reported related to potential risks in the risk management plan.

Study Number: 201234

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Study Center ID: 212947

Subject ID: (b) (6)

Randomization Number: UNKNOWN

Case ID: (b) (6)

Suspect Products: Flu Seasonal QIV Quebec

Serious Events: Febrile convulsion

Non-Serious Events:

Narrative: This 2-year-old male subject was enrolled in a blinded study titled Immunogenicity and safety study of GSK Biologicals' quadrivalent influenza vaccine (GSK2282512A) compared to Fluzone Quadrivalent in children 6 to 35 months of age. The subject received the 1st dose of Flu Q-QIV vs Fluzone Quadrivalent (intramuscular) on (b) (6), for prophylaxis.

On (b) (6), 88 days after receiving Flu Q-QIV vs Fluzone Quadrivalent, the subject developed severe - grade 3 febrile seizure. Serious criteria included GSK medically significant and clinically significant/intervention required. The outcome of febrile seizure was recovered/resolved on (b) (6)

The investigator considered that there was no reasonable possibility that the febrile seizure may have been caused by Flu Q-QIV vs Fluzone Quadrivalent.

Investigator Text:
The subject was at the Emergency Room on (b) (6) presenting high fever. The mother said that the child had a fever seizure. The medical records were requested to the hospital for more information. The child did not get hospitalized. The Principal Investigator assessed the Serious Adverse Event is not related to the Investigational Product.
Medical records received from ER and the History of present illness was: The patient presents with fever and febrile seizure. The fever began this am, with a miximun temperature of 40.3 degrees celcius, taken at axillary, fluctuating in intensity, there were occasional prior episodes, PT wax DX with OM two weeks ago and was treated with three doses of Rocephin, as well as a 10 days course of ABX(parents do not remember the name of ABX). And PT in daycare. Started with cough and runny nose/nasal congestion yesterday. The febrile seizure began in the ED, single episode, described as generalized, less than 3 minutes, with a maximum temperature of 102.3 degrees fahrenheite, in triage, taken axillary, there were no prior episodes and no family history of febrile seizure. Dad reports FMHX of epilepsy. Complaint:2 loose yesterday. Non bloody, cough and runny nose. The risk factor is day care. There are associated symptoms including rhinorrhea, congestion, nasal congestion, cough and diarrhea.
Patient was rushed into our resus room as he was seizing with the fever of 102.3 axillary. Monitors were placed on patient as well as oxygen and air way open and attended to. The seizure lasted approx. 2 minutes in the resus room and possibly one minute prior,. The seizure was generalized in nature. A PIV was placed. Blood work drawn including blood cx. No seizure medication were given. No foaming at the mouth. Patient recovered without complication and was brought to an exam room for further evaluation and observation.