From: (b)(6)
Sent: Fri, 16 Oct 2009 10:23:28 -0400
To: Destefano, Frank (CDC/OD/OCSO)
Cc: Markowitz, Lauri (CDC/CCID/NCHHSTP)
Subject: Fw: CERVARIX approved in US
Attachments: 20091016095208.pdf

Dear Frank:

Attached is the FDA approval letter for Cervarix. We thought it might be useful for you to see what post-marketing studies they have requested.

Best regards,
Peggy

Margaret B. Rennels, M.D.
Executive Director, U.S. Scientific Vaccine Policy
GlaxoSmithKline Biologicals
Suite800
1050 K St. NW
Washington, D.C. 20001
office: 202-715-1026
(b)(6)
fax 202-715-1001
(b)(6)

From: Saddier, Patricia
Sent: Mon, 17 May 2010 20:34:35 -0400
To: Destefano, Frank (CDC/OID/NCPDCID)
Cc: Liaw, Kai-Li
Subject: FW: VSD question
Attachments: ACIP_HPV_Oct 2008.pdf

Dear Frank,

The lead epidemiologist for Gardasil (HPV4 vaccine) at Merck, Dr. Kai-Li Liaw (copied on this e-mail), has a couple of questions on the VSD study for GARDASIL and I thought you might be able to help us.

In the attached ACIP presentation made by the VSD study investigators in October 2008, slide 6 lists the AEs of interest in the VSD study along with the time window for each. We are wondering what the last column entitled "first in what period?" represents. For most AEs, it seems to match pretty closely the time window of interest, but we were wondering why for VTE, the window was 42 days when the "period" column indicates "1 year".

We would greatly appreciate it if you could help us with this question or direct us to some one who could.

Thank you in advance for your help.

Kind regards,
Patricia

Patricia Saddier, MD PhD
Senior Director, Epidemiology
Merck Research Laboratories
351 North Sumneytown Pike, UG1D-60
North Wales, PA 19454-25059
(b)(6)

From: Liaw, Kai-Li
Sent: Monday, May 17, 2010 12:14
To: Saddier, Patricia
Subject: VSD question

Hi Patricia,

Per our discussion, here's the slide deck, please refer to page 6. Thanks so much!

<<ACIP_HPV_Oct 2008.pdf>>

Kai-Li

Kai-Li Liaw
(b)(6)

Vaccine Safety Datalink Project: Monitoring the Safety Of Quadrivalent Human Papillomavirus Vaccine (HPV4)

Advisory Committee on Immunization Practices Meeting, October 22, 2008

Julianne Gee, MPH[1]

Allison Naleway, PhD[2]

Irene Shui, MPH[3]

[1]Center for Disease Control and Prevention, Atlanta GA
[2] Kaiser Permanente Northwest, Portland OR
[3] Harvard Pilgrim, Boston MA

Vaccine Safety Datalink (VSD)

Collaboration between CDC and 8 managed care organizations

Data from 8.8 million members captured annually (3% of US population)

Vaccine Safety Datalink (VSD)

- Established in 1990 to improve the evaluation of vaccine safety through use of active surveillance and epidemiological studies
  - Addressed limitations of the Vaccine Adverse Event Reporting System (VAERS)
  - Responded to needs identified by two Institute of Medicine reports
- VSD tests hypotheses suggested by VAERS reports and pre-licensure trials

Rapid Cycle Analysis (RCA)

- Alternative to traditional post-licensure vaccine safety study methods, which generally take years to complete
- RCA Studies:
  - Tests specific hypotheses with well-defined outcomes
  - Each week, evaluate the number of events in vaccinated persons
  - Compare it to the expected number of events based on a comparison group
    - Historical or concurrent
  - Weekly analyses with statistical adjustment for multiple looks

Lieu TA, et al. Real-time vaccine safety surveillance for the early detection of adverse events. Med Care. 2007 Oct;45:S89-95.

HPV4 RCA Study

- Objective: Identify associations between HPV4 and a pre-specified list of adverse outcomes in females age 9-26 years
- 7 participating VSD sites
- Females 9-26 yrs
  - Youth: 9-17 yrs
  - Adults: 18-26 yrs
- Data from August 20, 2006-July 20, 2008
  - Allow for late arriving data
- Monitor until:
  - Youth: 350,000 doses
  - Adults: 150,000 doses

HPV RCA Outcomes

Outcome	Exposure window (days)	Medical Setting	First in what period?
Guillain Barré Syndrome (GBS)	1 to 42	All	42 days
Seizures	0 to 42	Inpatient, ED	42 days
Syncope	0	All	2 days
Appendicitis	0 to 42	Inpatient, ED	42 days
Stroke	0 to 42	Inpatient, ED	42 days
Venous Thromboembolism (VTE)	1 to 42	All	1 year
Anaphylaxis	0 to 2	All	2 days
Other Allergic rxns	0 to 2*	All	42 days

*exclude day 0 if clinic setting

HPV4 RCA: Cohort

- Exposed cohort: Females 9-26 years receiving HPV4
- Historical comparison group (Poisson Max SPRT*):
  - Background rates of select outcomes for females 9-26 yr of age:
    - Enrolled in a participating VSD site
    - Other data sources (Health Care Utilization Project)
  - Outcomes: GBS, Appendicitis, Stroke, VTE
- Concurrent comparison group (Flex Exact Sequential Analysis)
  - Females in the same age range who had a preventative or vaccination visit during the same time period as the exposed group
  - Outcomes: Seizures, Syncope, Allergic Reactions
- No formal comparison being performed for anaphylaxis

* Poisson Maximum Sequential Probability Ratio Test

Poisson MaxSPRT Analysis

- Observed number of events compared to expected number from historical group
- Association ("signal") detected if critical value of log likelihood ratio (LLR) exceeded

Kulldorff M, et al. A Maximized Sequential Probability Ratio Test for Drug and Vaccine Safety Surveillance. *Submitted for Publication.*

Flexible Exact Sequential Analysis

- Threshold p-value is established that accounts for continuous monitoring
- Observed number of events compared to expected number from concurrent group
  - matched by the variables of interest
- Association ("signal") detected if weekly p-value is less than the threshold p-value

Preliminary Results: HPV4 Doses Administered

- Total HPV4 doses administered (through week July 20, 2008): 377,960
  - Youth: 259,986
  - Adults: 117,974
- Total utilization by dose:
  - Dose 1: 50.4%
  - Dose 2: 31.5 %
  - Dose 3: 18.1%

Preliminary Results: Historical Comparison - Adults

Outcome	Events Observed	Events Expected	RR	Log Likelihood Ratio (LRR)	Critical Value of LRR	Signal ?
GBS	0	0.31	0.00	0.00*	2.86	No
Appendicitis	21	21.12	0.99	0.00*	3.68	No
Stroke	3	1.58	1.91	0.51	2.97	No
VTE	7	10.11	0.69	0.00*	3.57	No

* LRR is automatically set to zero when RR < 1

Preliminary Results: Concurrent Comparison- Adult

Outcome	Exposed Cases	Unexposed Cases	Comparison visit	RR	Binomial Test P-Value	Threshold P-Value	Signal ?
Seizure	18	26	PC	1.18	0.39	0.02	No
Syncope	129	57	Vac	0.54	0.99	0.03	No
Other Allergic reactions	32	7	Vac	1.45	0.26	0.02	No

Total preventative care (PC) comparison visits: 211,878
Total vaccination (Vac) comparison visits: 34,917

Preliminary Results: Historical Comparison-Youth

Outcome	Events Observed	Events Expected	RR	Log Likelihood Ratio (LRR)	Critical Value of LRR	Signal ?
GBS	0	0.50	0.00	0.00*	2.86	No
Appendicitis	33	41.99	0.79	0.00*	3.86	No
Stroke	0	0.84	0.00	0.00*	2.97	No
VTE	7	3.57	1.96	1.28	3.25	No

* LRR is automatically set to zero when RR < 1

Preliminary Results: Concurrent Comparison- Youth

Outcome	Exposed Cases	Unexposed Cases	Comparison Visit	RR	Binomial Test P-Value	Threshold P-Value	Signal ?
Seizure	34	14	PC	1.13	0.45	0.02	No
Syncope	452	120	Vac	0.99	0.56	0.04	No
Other allergic reactions	44	24	Vac	0.75	0.85	0.02	No

Total comparison preventative care (PC) visits: 141,329
Total comparison vaccination (Vac) visits: 106,252

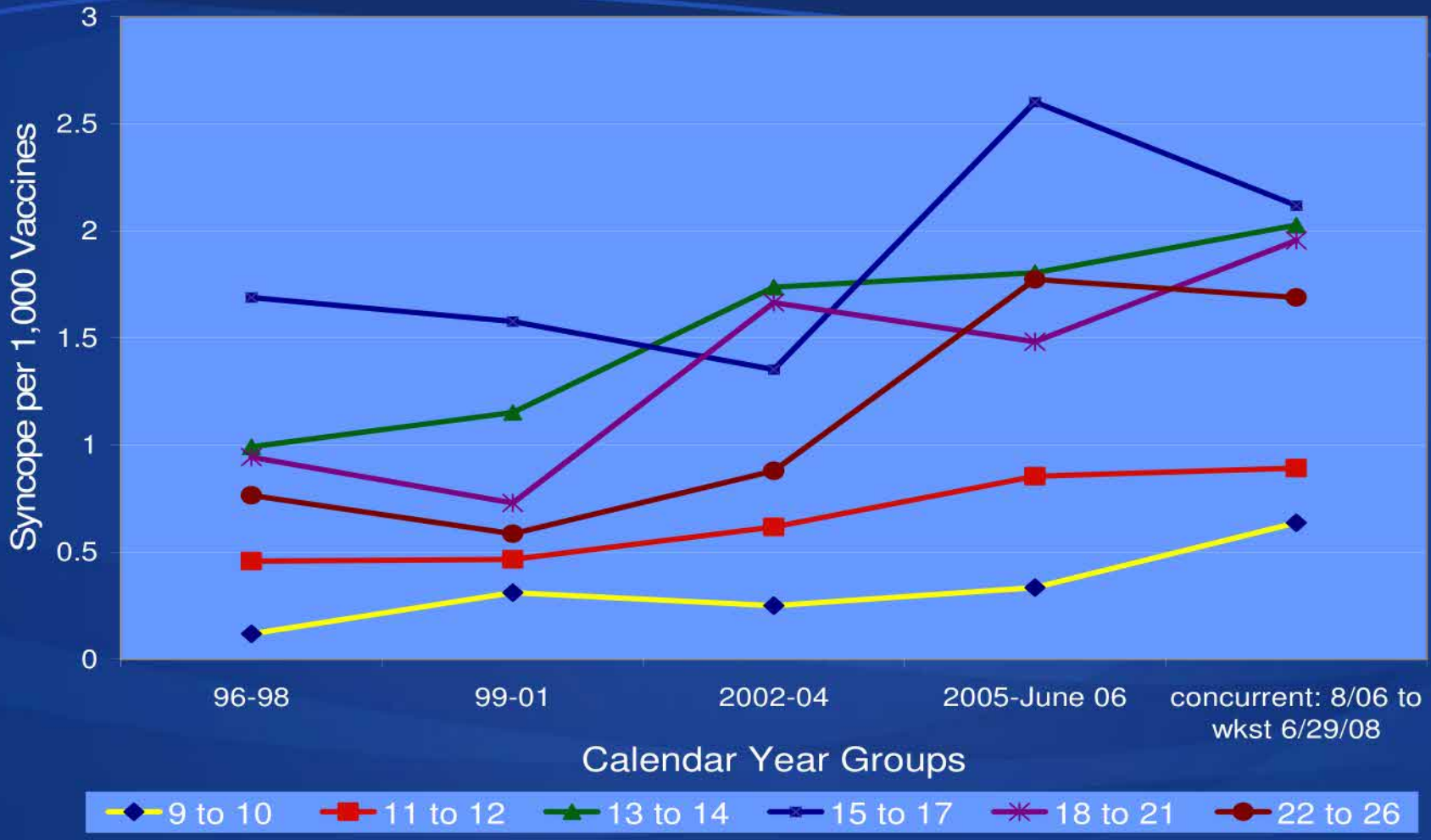
Syncope Logistic Regression Results: Concurrent Comparison Group

	Age and Secular Trend Adjustment *		
	RR	95% CI	p-value
Youth	0.99	0.80, 1.22	0.93
Adult	0.66	0.48, 0.91	0.01
Combined	0.88	0.74, 1.05	0.16

*Age adjusted by 2-3 year groups: 9-10, 11-12, 13-14, 15-17, 18-19, 20-21, 22-23, 24-26

Years of analysis: 8/20/06-6/29/08

Syncope per 1000 Vaccines Visits
Following Td, Tdap, Menactra, and Varicella



Anaphylaxis

- # of events youth in automated data:
  - Exposed: 8
  - Comparison group: 9
- # of events among adults in automated data:
  - Exposed: 7
  - Comparison group: 2
- Chart confirmed number of vaccine-related cases:
  - Youth: 0
  - Adult: 0
- Rate:
  - 0 cases/million doses (95% CI: 0.0 -9.76)
- Background rate:
  - 1.53 cases/million doses (95% CI: 0.04-8.52) *

* Bohlke K, et al. Risk of Anaphylaxis after Vaccination of Children. Pediatrics 112(4); 2003

Additional monitoring

- Weekly monitoring ongoing since July 20, 2008
- Highlighted findings:
  - 1 GBS case identified
    - Preliminary chart review conducted
      - Not a confirmed exposed case
  - Limited power at this time to rule out a true risk of GBS following HPV4
    - Based on a probability of observing 0 cases per 420,000 doses, we are unable to rule out a RR of less than 5

Major Findings and Next Steps

- With >375,000 doses administered, VSD active surveillance did not find statistically significant risk for any of the pre-specified adverse events after vaccination for either age group
- No major increase in rate of anaphylaxis following HPV4 as compared to previous studies
- Continue to monitor outcomes until reach upper limits for adverse events or until reach dose limit
- Continue to monitor rare adverse events
  - GBS, VTE, stroke

Acknowledgements

- Eric Weintraub, MPH
- James Baggs, PhD
- Tracy Lieu, MD
- Ned Lewis, MPH
- Bruce Fireman, MA
- Martin Kulldorff, PhD
- Data Coordinating Center at Harvard Pilgrim
- VSD Project

Disclosure

- **VSD principal investigators for this study wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters**

From: Peggy Rennels
Sent: Fri, 1 Jul 2011 11:47:30 -0500
To: Pickering, Larry (CDC/OID/NCIRD);Wharton, Melinda (CDC/OID/NCIRD);michael brady (b)(6) Kroger, Andrew (CDC/OID/NCIRD);Bell, Beth (CDC/OID/NCEZID);Bridges, Carolyn (CDC/OID/NCIRD);Whitney, Cynthia (CDC/OID/NCIRD);Destefano, Frank (CDC/OID/NCEZID);Goeff evans (gevans@HRSA.gov);Wallace, Gregory (CDC/OID/NCIRD);Ortega-Sanchez, Ismael (CDC/OID/NCIRD);Seward, Jane (CDC/OID/NCIRD);Santoli, Jeanne (CDC/OID/NCIRD);Liang, Jennifer L. (CDC/OID/NCIRD);Bresee, Joseph (CDC/OID/NCIRD);Iskander, John (CDC/OD/OADS);jon temte (b)(6) Rodewald, Lance (CDC/CGH/GID);Markowitz, Lauri (CDC/OID/NCIRD);Grohskopf, Lisa A. (CDC/OID/NCIRD);Cortese, Margaret (CDC/OID/NCIRD);martin meltzer (QZMA4@cdc.gov);Cox, Nancy (CDC/OID/NCIRD) (CTR);Harpaz, Rafael (CDC/OID/NCIRD);roger suchyta (b)(6) roger suchyta (b)(6) sarah landry (landrys@niaid.nih.gov);Uyeki, Timothy M. (CDC/OID/NCIRD);Clark, Thomas A. (CDC/ONDIEH/NCCDPHP);Murphy, Trudy (CDC/OID/NCHHSTP) (CTR);Parashar, Umesh (CDC/OID/NCIRD)
Cc: Leonard Friedland;Leonard Silverstein
Subject: New CDC liasons

Dear All:

I have decided to leave GSK. It have been an interesting and educational experience, but it is simply time for me to move on.

Leonard Friedland, VP Clinical and Medical Affairs will assume the role of primary GSK contact with CDC, ACIP, and COID. If you are unable to contact Dr. Friedland, reach out to Leonard Silverstein, Head of Medical Affairs . You will find them both knowledgeable and helpful. Their e-mails are above.

I have enjoyed working with all of you and will sorely miss our interactions.

Margaret B. Rennels, M.D.
Executive Director
U.S. Vaccine Scientific Policy

(b)(6)

From: Sylvester, Gregg C
Sent: Mon, 4 Jun 2012 13:52:14 +0000
To: Vellozzi, Claudia (CDC/OID/NCEZID)
Cc: Destefano, Frank (CDC/OID/NCEZID);Slavin, Dorothy
Subject: RE: Pfizer (PCV13) Safety

Claudia:

I hope you are doing well. I'm just checking in with you because, I will be traveling for most of the month of June. No worries, I have copied Dorrie Slavin on this e-mail. She is a medical colleague of mine and can be your contact person when you (CDC) are prepared to share the data with us (Pfizer). Dorrie has taken the lead on drafting our response back to the FDA, so she is intimately involved in the issue.

You have her e-mail address (up above) and her office phone is (b)(6) **. Please don't hesitate to call her.**

It is our hope that we can pull a few of our medical folks together to hear your findings.

Thanks again,
Gregg

Gregg C. Sylvester, MD, MPH
Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group
Pfizer Inc.

From: Vellozzi, Claudia (CDC/OID/NCEZID) [mailto:bno1@cdc.gov]
Sent: Wednesday, May 16, 2012 9:34 AM
To: Sylvester, Gregg C
Cc: Destefano, Frank (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Gregg
The analysis should be completed the first week of June and I suspect we will be sharing with a variety folks shortly after, including you.

Claudia Vellozzi, MD, MPH
404-639-6175
404-944-2737

From: Sylvester, Gregg C [mailto:Gregg.C.Sylvester@pfizer.com]
Sent: Tuesday, May 15, 2012 5:58 PM
To: Vellozzi, Claudia (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Claudia:

How are you? Have you finished that wonderful Spring that Atlanta is famous for? Has Summer started? ;-)

I was wondering if your team (internal/external) has finished the VSD study on KD after PCV13 vaccination?

If so.....would you share the results with us (Pfizer)? If not.....do you know when it might be finished?

Thanks,
Gregg

Gregg C. Sylvester, MD, MPH
Global Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group
Pfizer Inc.

From: Vellozzi, Claudia (CDC/OID/NCEZID) [mailto:bno1@cdc.gov]
Sent: Wednesday, April 18, 2012 6:23 PM
To: Sylvester, Gregg C
Cc: Destefano, Frank (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

That shouldn't be problem
Claudia

From: Sylvester, Gregg C (b)(6)
Sent: Wednesday, April 18, 2012 5:41 PM
To: Vellozzi, Claudia (CDC/OID/NCEZID)
Cc: Destefano, Frank (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Claudia:

Thank you for updating me. I think that seems like a fair and prudent approach. We are reviewing all of our internal data also.

Would it be possible for your team to share the results with us (Pfizer) when you complete your analysis?

Thanks again,
Gregg

From: Vellozzi, Claudia (CDC/OID/NCEZID) [mailto:bno1@cdc.gov]
Sent: Wednesday, April 18, 2012 8:30 AM
To: Sylvester, Gregg C
Cc: Destefano, Frank (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Hi Gregg,
I just wanted you to know that I did discuss this with our counterparts at the FDA (so not Holly below) and they will share our update regarding the timeline for a final analysis for Kawasaki with Holly's group.
I hope this helps.
Thanks,
Claudia

From: Sylvester, Gregg C (b)(6)
Sent: Wednesday, April 11, 2012 9:59 AM

To: Vellozzi, Claudia (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Claudia & Tom:

Holly Wieland (b)(6) is the person that we had spoken to at CBER within the FDA. Please don't hesitate to tell her that you have spoken with us. We are not trying to hide anything.

It is not our intent or desire for you to get involved with their regulatory decision process. We are only asking that you make Holly (CBER) aware that your VSD study is still ongoing and when you believe your analysis will be finished.

Pfizer is asking for more time to gather internal data and hopefully review the VSD before we commit to a language change in our label. We are hoping that good science and reliable data will shape our PCV13 label.

Please let me know if I can provide you any other further information.

Thanks you,
Gregg

Gregg C. Sylvester, MD, MPH
Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group
Pfizer Inc.

From: Vellozzi, Claudia (CDC/OID/NCEZID) [mailto:bno1@cdc.gov]
Sent: Monday, April 09, 2012 4:25 PM
To: Shimabukuro, Tom (CDC/OID/NCEZID); Sylvester, Gregg C
Subject: RE: Pfizer (PCV13) Safety

Gregg,
Just to clarify—we can give the FDA our timeline for final results, etc but we do not provide advice for their regulatory decisions. We are happy to discuss our current findings and timeline for final analysis with the FDA.
Thanks.

Claudia Vellozzi, MD, MPH
Deputy Director, Immunization Safety Office, CDC
404-639-6175
cell: 404-944-2737

From: Shimabukuro, Tom (CDC/OID/NCEZID)
Sent: Monday, April 09, 2012 4:00 PM
To: Sylvester, Gregg C
Cc: Vellozzi, Claudia (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Okay, thanks.
Tom

From: Sylvester, Gregg C (b)(6)
Sent: Monday, April 09, 2012 3:00 PM

To: Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Tom & Claudia:

Thanks again for speaking with me last week. I understand that it's too soon to sit down and share with us the results from SCKP, however, I do want to accept your offer of talking with the FDA.

I have discussed it with my colleagues at Pfizer and we would appreciate it if you would be willing to follow up with the FDA and suggest that it is premature to add KD to our label. We are reexamining our internal data and would like to see the results of the VSD (SCKP) prior to further discussion.

I will get you the name of our contact at the FDA. It might very well be the same person you are sharing information with.

Thanks again,
Gregg

P.S. I don't have Claudia's e-mail. Can you please forward or discuss with her. Thx

Gregg C. Sylvester, MD, MPH
Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group
Pfizer Inc.

From: Shimabukuro, Tom (CDC/OID/NCEZID) [mailto:ayv6@cdc.gov]
Sent: Thursday, April 05, 2012 2:10 PM
To: Sylvester, Gregg C
Subject: RE: Pfizer (PCV13) Safety

Gregg,

I'll set up a call for next week. Maybe Tuesday morning, but we need to get S. California Kaiser on the line, so that may take a little time to organize. Is Tuesday morning good for you?

Tom

From: Sylvester, Gregg C (b)(6)
Sent: Thursday, April 05, 2012 1:52 PM
To: Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Tom:

Thanks for the information. It seems from my internal discussions that the FDA has a shorter timeframe. I am under the impression that they are looking for something from us sooner. Is it possible to have a preliminary meeting in the next week or two and meet again in a month when the data is final?

Gregg

Gregg C. Sylvester, MD, MPH
Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group

Pfizer Inc.

From: Shimabukuro, Tom (CDC/OID/NCEZID) [mailto:ayv6@cdc.gov]
Sent: Thursday, April 05, 2012 1:44 PM
To: Sylvester, Gregg C
Subject: RE: Pfizer (PCV13) Safety

Gregg,

The VSD evaluation of the association between PCV13 and Kawasaki disease is ongoing, but close to completion and we should have final results either later this month or in May. We can do a briefing for the Pfizer staff to present the final data. Maybe we can tentatively schedule something for early May. Will that work for you? Let me know.

Tom

From: Sylvester, Gregg C (b)(6)
Sent: Thursday, April 05, 2012 9:55 AM
To: Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Thank you very much.....

Gregg C. Sylvester, MD, MPH
Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group
Pfizer Inc.

From: Shimabukuro, Tom (CDC/OID/NCEZID) [mailto:ayv6@cdc.gov]
Sent: Thursday, April 05, 2012 9:54 AM
To: Sylvester, Gregg C
Subject: RE: Pfizer (PCV13) Safety

Gregg,

I am aware of the ongoing PCV13 surveillance in VSD, but not familiar with the details for Kawasaki. Let me check with the VSD team and get back to you on that.

Tom

From: Sylvester, Gregg C (b)(6)
Sent: Thursday, April 05, 2012 7:54 AM
To: Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: RE: Pfizer (PCV13) Safety

Tom:

Thank you for the follow up. I will share this analysis with my colleagues here.

I was actually calling you about another issue. FDA mentioned that the CDC saw a transient signal with PCV13 for Kawasaki Disease in VSD. We have not seen any type of signal and would like to learn more. Can you direct me to the right person to discuss this matter?

Gregg

Gregg C. Sylvester, MD, MPH
Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group
Pfizer Inc.

From: Shimabukuro, Tom (CDC/OID/NCEZID) [mailto:ayv6@cdc.gov]
Sent: Wednesday, April 04, 2012 4:43 PM
To: Sylvester, Gregg C
Subject: RE: Pfizer (PCV13) Safety

Gregg,

Attached is the final VSD analysis of the 2010-11 febrile seizure signal. This really summarizes the data that was presented to ACIP and CDC leadership and was the basis for our public communications on febrile seizure risk and the determining factor for not recommending any changes in the schedule. It is the same data that was presented to Pfizer and Sanofi back in the fall of 2011, so I think you have seen the relevant data.

We have been monitoring for seizures for this influenza season in VSD, but not with the same intensity as last season because TIV didn't change from 2010-11 and recommendations didn't change and we already consider the signal to be assessed and quantified. The findings for this influenza season are consistent with what we saw in 2010-11 and this is not unexpected. This information was communicated to ACIP at the last meeting.

Let me know if you still want to discuss this. Thanks.

Tom

Tom Shimabukuro, MD, MPH, MBA
CDR, U.S. Public Health Service
Senior Medical Officer
Immunization Safety Office
Centers for Disease Control and Prevention (CDC)
1600 Clifton Road, MS D-26, Atlanta, GA 30333

Phone: 404-639-4848
Fax: 404-639-8834
Email: TShimabukuro@cdc.gov

From: Sylvester, Gregg C [mailto:Gregg.C.Sylvester@pfizer.com]
Sent: Wednesday, April 04, 2012 11:22 AM
To: Shimabukuro, Tom (CDC/OID/NCEZID)
Subject: Pfizer (PCV13) Safety

Tom:

Remember me? We spoke last year, regarding TIV/PCV13 and febrile seizures.

I have a new question with regards to the FDA and our PCV13 label. The FDA is telling us that they have seen some VSD data that has not been shared with us.

Could we chat for a few minutes today?

Thanks,
Gregg

P.S. I know the world of Public Health is a small world……but I didn't put 2 + 2 together. We have met before……..through your (b)(6)

Gregg C. Sylvester, MD, MPH
Medical Lead for Prevenar & Prevenar 13
Pediatric Vaccines
Medicines Development Group
Pfizer Inc.

From: Guillermo Herrera Taracena
Sent: Wed, 24 Aug 2011 11:43:07 -0500
To: Destefano, Frank (CDC/OID/NCEZID)
Subject: VSD related question

Dear Frank,

I hope this email finds you well. As you have surely heard, narcolepsy is an issue hot in the news for GSK. Global Epidemiology in Brussels is exploring possibilities for a study looking into narcolepsy seasonal trends in the US and I was asked to look into the VSD. As we worked in the past with VSD, I decided to first seek for your opinion and depart from there. The Influenza Group at GSK will be visiting the CDC on September 22nd and this could be an opportunity to further explore any alternatives there could be. Let me know and if you prefer, we can talk on the phone at a date and time that is of your convenience.

All the best,

Guillermo Herrera Taracena, MD, MBA
GlaxoSmithKline
Medical Affairs
Director Influenza Vaccines
(b)(6)

From: Peggy Rennels
Sent: Fri, 4 Feb 2011 10:09:47 -0600
To: Destefano, Frank (CDC/OID/NCEZID)
Subject: ACIP Safety Office Update

Dear Frank:

Is there any information that you want/need from GSK for the ACIP session on febrile seizures?

Kind regards,
Peggy

Margaret B. Rennels, M.D.
Executive Director
U.S. Vaccine Scientific Policy

(b)(6)

From: (b)(6)
Sent: Fri, 28 Jan 2011 08:11:24 -0500
To: Destefano, Frank (CDC/OID/NCEZID)
Subject: FW: BioSIG Meeting Minutes - 26Jan2011
Attachments: ISPE 2010_symposium abstract.doc

Dear Frank,

I hope you are doing well. Is there someone in VSD team who would be willing to put together a symposium for vaccines in upcoming ICPE 2011? Please, see some ideas below in e-mail exchange.

Best regards,
Alena

Hello Everyone,

The February 16th abstract deadline is quickly approaching and until then we will be meeting weekly to complete our submission. At the last meeting we discussed the approach of expanding on the Biosimilars FDA docket submission if possible and finding a topic that is novel, but not too distant.

Topics discussed include biologics in the context of hot topics including:

* Biosimilar legislation - EU experience vs. US Status and Expectations

* OMOP including biologics

* Biologics and the mini sentinel project

* Biologics from a pharmacoepidemiology prospective - what do we need to know?

We would like to hear from everyone with ideas/topics for a workshop or symposium. If you have a suggestion, please submit suggestions to me with a statement on the topic and a few bullets about potential speakers and areas to address. I will send out a list of topics before the meeting for everyone to review.

Thanks and speak with you soon,

Neal Grabowski

(b)(6)

From: Wise, Robert [mailto:Robert.Wise@fda.hhs.gov]
Sent: Thursday, January 27, 2011 4:46 PM
To: Khromava, Alena (sanofi pasteur); (b)(6)
(b)(6)
Cc: rchen@cdc.gov; (b)(6)

Subject: RE: BioSIG Meeting Minutes - 26Jan2011

I'm sorry that I can't volunteer to help with this abstract idea.

CDC employed lot identifiers (aka "numbers") to classify VSD vaccinations by thimerosal -- lots produced before vs. after removal of thimerosal. That experience might be appropriate for this abstract.

From: (b)(6)
Sent: Wednesday, January 26, 2011 2:49 PM
To: (b)(6)
Cc: rchen@cdc.gov; (b)(6) Wise, Robert
Subject: RE: BioSIG Meeting Minutes - 26Jan2011

Dear Neal and Joanna,

Thank you for organizing a teleconference today to discuss on preparations towards symposium submission on topic "How does vaccine experience impact biosimilars for better or worse?". As I indicated on the call SP does not have an extensive experience of identifying our product using lot numbers in large population databases. I am copying my colleagues from GSK Bio and Merck, as well Bob Wise and Bob Chen to see if they would be willing to step in to prepare an abstract for the symposium.

Unfortunately, in the next two weeks I have a very busy schedule and will be out of the office next Wednesday and not able to attend the next group's meeting.

Kind regards,
Alena

From: Grabowski, Neal (b)(6)
Sent: Wednesday, January 26, 2011 1:11 PM
To: Khromava, Alena (sanofi pasteur); Anders Sundstrom; Bert Leufkens; Bob Chen; Bob Wise; Carlos Grijalva; Dianlin Guo; Douglas Watson; Earl Goehring; Erica Velthuis; Giezen, T.J. ; Grabowski, Neal; Gumieniak, Olga; Haas, Joanna; Hans Petri; Hui Zhang; Jane Porter; Jeff Curtis; Judith Jones; Jyotsna Mehta (h); Marie-Josee Martel; Marlene Hoynck van Papendrecht M.Sc., M.D., Ph.D.; Meg Richards; Melanie Harrison; Michael Taylor; Beigeaud, Myriam (sanofi pasteur); Nils Feltelius; Pavel Napalkov; Peter Aquino; Priscilla Velentgas; Quazi Ataher; Rizwan Ahmad; Sabine Straus; Sean Zhao; Stephen Motsko; Stephen Paul Motsko; TORBJORN CALLREUS; Wei Dong; Wenjun Jiang; Will Dixon; Will Dixon (alt); Xuehua Ke; Zhiping Huang
Cc: Haas, Joanna
Subject: BioSIG Meeting Minutes - 26Jan2011

Hello Everyone,

Thank you to those who were able to join us on this morning's teleconference – there was a lot of great discussion and progress made toward our symposium and workshop submissions for ICPE 2011.

The symposium will most likely center on biosimilars in the context of current hot topics. It will likely include an EU prospective, current initiatives (OMOP, mini-sentinel, NCEP, etc) and current

status/next steps in the U.S. Jane Porter has volunteered to draft an outline for discussion next week.

The proposed workshop topic is 'How does the vaccine experience impact biosimilars for better or worse?' There are many parallels between vaccines and biosimilars including multiple manufacturers and variants of a given product, need for identification of agent and quick responses to potential safety issues. Joanna and Alena Khromava will work on a draft submission and reach out to potential speakers.

As always, we welcome anyone who would like to contribute to the abstracts and both Joanna and I are available to help in any way we can.

I have attached one of last year's submissions to give an idea what is involved in completing the abstract. The guidelines from the ISPE website on symposium and workshop abstracts can be found below:

GUIDE FOR CONTRIBUTED WORKSHOP OR SYMPOSIUM

Workshop and Symposia are 90-minute sessions on a specific topic organized by the presenter. Organizers of workshop/symposia are strongly encouraged to seek a fair balance and a reasonable representation of all views on a topic.

The organizer/submitter should provide as much detail as possible including the names of panelists/faculty on the abstract submission. The Chair, Scientific Program Committee, must approve any change to the panel/participants after the abstract/proposal is accepted. The organizer/submitter is responsible to notify the Chair, Scientific Program Committee and ISPE Office of any change in the panel/participants. The Chair will respond directly to the organizer/submitter.

- **Workshop:** A workshop is a small, interactive training session addressing a specific topic. It is intended to teach the attendee either through examples or through highly interactive discussion. It would be rare to present new study findings in a workshop unless the study uncovered some new methodology, data source, or technique that itself is the focus of the training. Seating will be on a "first-come, first-served" basis.

  The author must state how the workshop will be interactive and how attendees could participate in the session.

- **Symposium:** A symposium is an intellectually and content focused presentation(s) or consensus generating discussion on a well-defined subject. The intent is to provide the attendee with a concentrated exposure to a topic without necessarily presenting new data or study findings. Unlike the workshop, a symposium usually is presented in the more classical style of presentation and open debate/questions or consensus discussion.

  Format - Please use the following headings when proposing a workshop or symposium:

  1. **Topic**

2. **Title**

3. **Background:** One or two sentences that describe the importance or relevance of the topic.

4. **Objectives:** The main objectives of the workshop/symposium should be explicitly stated (e.g., "To review analytic techniques for the analysis of intermittent exposures."). There should also be a statement regarding who would benefit by attending the session (e.g., "Researchers involved or seeking additional expertise in the analysis of large claims databases.")

5. **Description:** A clear description of the workshop/symposium.

6. **List of Speakers**

I will schedule a call next Wednesday with WebEx to review the draft submissions.

Thanks,
Neal

Neal Grabowski

Associate
Global Patient Safety and Risk Management
Genzyme Corporation
675 West Kendall St.
Cambridge, MA 02142
(b)(6)

26th International Conference on Pharmacoepidemiology and Therapeutic Risk Management

Abstract Number: 750883

Submission Type: Workshop/Symposium

Presenting/Contact Author: Thijs Giezen

Department/Institution: Utrecht Institute for Pharmaceutical Sciences

Address: Sorbonnelaan 16

City/State/Zip/Country: Utrecht, Netherlands

Phone: +31302539958 **Fax:** **E-mail:** t.j.giezen@uu.nl

Subfield within pharmacoepidemiology: Classical pharmacoepidemiology

Does your contribution focus on a specific exposure? Yes
Choices:
Other

Does your contribution focus on a specific outcome? No

Does your contribution focus specifically on methodological aspects? Yes
Choices:
Other

Does your contribution focus on a specific population? No

Does your contribution fit with the interests of one of the SIGs? Yes
Choices:
Biologics

Presentation format: Symposium only

Disclosure: None

Presentation Release - If my abstract is selected for presentation, I give ISPE permission to post my presentation, which will be given at ICPE 2010 in the Members Only section of the ISPE website after the ICPE. Yes

Title: Ascertaining the use of biologics (Biologics SIG symposium)

Thijs Giezen, PharmD[1,2], Judith Jones, MD,PhD[3], Will Dixon, MRCP,PhD[4], Michael Taylor, PharmD,PhD[5], Bert Leufkens, PharmD,PhD[1,2], and Earl Goehring, BA[3]. [1]UIPS, Utrecht, Netherlands; [2]Medicines Evaluation Board, The Hague, Netherlands; [3]The Degge Group Ltd., Arlington, United States; [4]University of Manchester, Manchester, United Kingdom; and [5]Genentech, San Francisco, United States.

Background: Biologics have specific characteristics, which might complicate their

exposure ascertainment and consequently pharmacoepidemiological studies.

Objectives: To discuss challenges in the exposure ascertainment of biologics and solutions for some of the faced problems which is of interest to researchers, industry and regulators working in this emerging field.

Description: 1. Why is a specific approach for the exposure assessment of biologics needed? – Thijs Giezen
This first presentation will focus on the characteristics of biologics and exposure assessment being a particular challenge.

2. Estimating exposure based on production and sales information - Judith Jones
Logistics of calculating exposure, given the many biologics available with different dosage regimens and different indications, will be discussed in this presentation.

3. Differences in coding/identification of biologics: US and EU perspectives - Michael Taylor/ Will Dixon
Coding/ identification of biologics differs among data sources which complicates the assessment of exposure to biologics. This will be discussed from an US and an EU perspective.

4. Differences in exposure among countries - Bert Leufkens
Differences exist among countries at which moment and at what moment in time treatment with biologics should be initiated and/ or stopped. These policy interventions influence the exposure to biologics among countries, which will be discussed in this presentation.

Chairs: Earl Goehring and Thijs Giezen