



Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

January 27, 2021

Elizabeth Brehm
Siri & Glimstad
200 Park Ave
17th Floor
New York, NY 10166
Via email: foia@sirillp.com

Dear Ms. Brehm:

This letter is regarding to your Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry (CDC/ATSDR) Freedom of Information Act (FOIA) request of October 23, 2020, assigned #21-00123-FOIA, for:

1. Any communications sent or received by Nancy Messonnier to or from representatives, directors, officers, or employees of GlaxoSmithKline (or Glaxo or GSK) while the Deputy Director or Director of the National Center for Immunization and Respiratory Diseases (NCIRD).
2. Any communications sent or received by Nancy Messonnier to or from representatives, directors, officers, or employees of Sanofi while the Deputy Director or Director of the National Center for Immunization and Respiratory Diseases (NCIRD).
3. Any communications sent or received by Nancy Messonnier to or from representatives, directors, officers, or employees of Merck & Co. while the Deputy Director or Director of the National Center for Immunization and Respiratory Diseases (NCIRD).
4. Any communications sent or received by Nancy Messonnier to or from representatives, directors, officers, or employees of Pfizer while the Deputy Director or Director of the National Center for Immunization and Respiratory Diseases (NCIRD).

We located 493 pages of responsive records (163 pages released in full, 162 pages released in part, and 168 pages withheld in full). After a careful review of these pages, some information was withheld from release pursuant to 5 U.S.C. §552 Exemptions (b)(4) and (b)(6).

EXEMPTION 4

Exemption 4 protects trade secrets and commercial or financial information obtained from a person that is privileged or confidential. The information withheld is commercial or financial information, such as proprietary information, and we have determined that the individual/s to whom this information pertains have a substantial commercial or financial interest in withholding it.

EXEMPTION 6

Exemption 6 protects information in personnel and medical files and similar files when disclosure would constitute a clearly unwarranted invasion of personal privacy. The information that has been withheld under Exemption 6 consists of personal information, such as phone numbers and email addresses. We have determined that the individual(s) to whom this information pertains has a substantial privacy interest in withholding it.

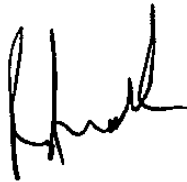
You may contact our FOIA Public Liaison at 770-488-6277 for any further assistance and to discuss any aspect of your request. Additionally, you may contact the Office of Government Information Services

(OGIS) at the National Archives and Records Administration to inquire about the FOIA mediation services they offer. The contact information for OGIS is as follows: Office of Government Information Services, National Archives and Records Administration, 8601 Adelphi Road-OGIS, College Park, Maryland 20740-6001, e-mail at ogis@nara.gov; telephone at 202-741-5770; toll free at 1-877-684-6448; or facsimile at 202-741-5769.

If you are not satisfied with the response to this request, you may administratively appeal by writing to the Deputy Agency Chief FOIA Officer, Office of the Assistant Secretary for Public Affairs, U.S. Department of Health and Human Services, Hubert H. Humphrey Building, 200 Independence Avenue, Suite 729H, Washington, D.C. 20201. You may also transmit your appeal via email to FOIARequest@psc.hhs.gov.

Please mark both your appeal letter and envelope "FOIA Appeal." Your appeal must be postmarked or electronically transmitted by April 27, 2021.

Sincerely,

A handwritten signature in black ink, appearing to read 'Roger Andoh', with a stylized, cursive script.

Roger Andoh
CDC/ATSDR FOIA Officer
Office of the Chief Operating Officer
(770) 488-6399
Fax: (404) 235-1852

Enclosures

21-00123-FOIA

From: nar5@cdc.gov
Sent: Fri, 16 Dec 2016 16:10:41 -0500
To: Patricia Novy
Subject: Re: Requesting your interest and availability for a GSK advisory board- Response Requested

Sure.

On Dec 16, 2016, at 4:05 PM, Patricia Novy <(b)(6)> wrote:

Dear Dr. Messonnier,

Thank you for the prompt reply. I completely understand your position and appreciate the offer for a subject matter expert to present some data. We would be delighted to take you up on that offer.

Would you be comfortable if I circle back with you in the New Year to coordinate?

Best wishes and happy holidays!

Patricia Novy, PhD

Medical Affairs Scientific Director -- Vaccines
US Medical Affairs

GSK

Email

Mobile

(b)(6)

From: Messonnier, Nancy (CDC/OID/NCIRD) [<mailto:nar5@cdc.gov>]

Sent: Friday, December 16, 2016 3:55 PM

To: Patricia Novy <(b)(6)>

Subject: RE: Requesting your interest and availability for a GSK advisory board- Response Requested

EXTERNAL

Ms. Novy,

In my current position, it would not be appropriate for me to participate in the advisory board. I certainly would be happy to have one of our subject matter experts present some of our data to the board.

Thank you.

Nancy Messonnier, MD
Director
National Center for Immunization and Respiratory Diseases
OID, CDC

From: Patricia Novy [mailto:(b)(6)]
Sent: Friday, December 16, 2016 3:12 PM
To: Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>
Subject: Requesting your interest and availability for a GSK advisory board- Response Requested

Dear Dr. Messonnier,

GSK is planning a two-day advisory board covering topics relevant to meningococcal vaccines, both licensed and investigational. On behalf of Kumaran Vadivelu, MD, Global Medical Affairs Lead for Neisseria/Meningococcal Vaccines and the US Neisseria Team, I would like to check your interest in participating in the advisory board and your potential availability for the below proposed dates. The location for the advisory board will be Atlanta, GA. Please reply and indicate with a "yes or no" your interest in participating in the advisory board and then indicate your availability with a "yes or no" for all the proposed dates. Since we need to reserve meeting space and hotel rooms, a response by Friday afternoon, December 23rd would be greatly appreciated. If you are unable to attend but would like to propose an alternate individual, please feel free to let me know your thoughts.

I am interested in participating in GSK's meningococcal vaccine advisory board (Yes/No):

I would be able to attend if held on the following dates:

March 28-29 (Yes/No):

March 30-31 (Yes/No):

April 6-7 (Yes/No):

Thank you very much and kind regards,
Trisha

Patricia Novy, PhD
Medical Affairs Scientific Director -- Vaccines
US Medical Affairs

GSK

Email

Mobile

(b)(6)

GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.

GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.

From: nar5@cdc.gov
Sent: Tue, 11 Jul 2017 13:58:13 -0400
To: (b)(6)
Subject: Re: Protein Sciences Press Release

Thank you for the heads up

On Jul 11, 2017, at 1:37 PM, "(b)(6)" <(b)(6)> wrote:

Greeting Nancy and Amanda-

Attached a press release for the announcement we are making today regarding our bid to purchase Protein Sciences.

Fast-moving and early in the process, I wanted to be sure you were aware of this initial step, and address any questions you might have.

I'd welcome any thoughts you might have -
Julian

<Protein Sciences PR v06072017 8h15CET FINAL.docx>

From: nar5@cdc.gov
Sent: Tue, 20 Feb 2018 20:27:07 -0500
To: Leonard Friedland
Cc: Shimabukuro, Tom (CDC/OID/NCEZID);Dooling, Kathleen L. (CDC/OID/NCIRD);Barbara Howe;Debora Rausch
Subject: Re: Len Friedland - GSK Vaccines

Got it. Thanks.

On Feb 20, 2018, at 6:24 PM, Leonard Friedland <(b)(6)> wrote:

Dear Nancy, Tom and Kathleen,

Tom thank you for the call today. Kathleen also called my colleague Deb Rausch.

We appreciate CDC noting during the ACIP meeting agency updates that reports have been received regarding Shingrix being administered SC, rather than IM, and patients not being instructed to return for dose 2 in the series; and that a MMWR "notes from the field" will be forthcoming to educate providers on proper administration and dosing schedule of Shingrix. We would like to make sure that you are aware that GSK has also received reports involving improper storage and use with diluent other than AS01 diluent supplied by GSK.

For your information, below is a copy of a letter GSK has provided to various organizations (eg. NFID, IAC, APhA, ACP) asking their assistance in reinforcing important education and communication about the storage, reconstitution and route of administration for Shingrix.

Nancy, GSK would appreciate if you would note the information in red below during the agency update which cover 1) proper storage requirements, 2) proper route of administration and 3) the need to reconstitute with the adjuvant (AS01) diluent supplied.

I will be at ACIP and welcome the opportunity to discuss further with you.

Best regards, Len

.....

Shingrix (Zoster Vaccine Recombinant, Adjuvanted), referred to as "RZV" by CDC, was approved for use by the US Food and Drug Administration (FDA) on October 20, 2017. As this new vaccine begins to reach clinics and pharmacies, and ultimately patients, we understand that this new vaccine is entering a medical community which is accustomed to the storage and administration requirements of another vaccine (Zoster Vaccine Live (ZVL)) for over a decade.

GSK has received a small number of reports from the field of maladministration of RZV. These reports of observed usage of RZV suggest that the root cause of

maladministration has been the utilization of the storage requirements and route of administration established for ZVL. Since ZVL and RZV have different storage requirements and routes of administration, we ask that you include in your communications regarding RZV the specific storage and administration requirements of Shingrix.

We ask for your support to help ensure that the **storage** and **administration** of RZV is executed according to the instructions outlined in the FDA approved product labeling. Please include and emphasize the following information in your education and communications on RZV to reinforce its proper storage, reconstitution and administration:

Storage, Reconstitution and Administration of RZV

- RZV is to be stored in the **REFRIGERATOR ONLY**. RZV must be discarded if frozen.
- RZV **MUST BE** reconstituted with the **ADJUVANT LIQUID SUSPENSION (AS01)** provided.
- RZV is to be administered **INTRAMUSCULARLY ONLY**. It is **NOT** to be administered subcutaneously.

Thank you for your review and consideration. We look forward to partnering with you to assure that RZV is stored, reconstituted and administered appropriately to maximize effectiveness and patient safety.

Leonard Friedland, MD
VP, Scientific Affairs and Public Health
GSK Vaccines

(b)(6)

GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.

From: nar5@cdc.gov
Sent: Wed, 24 Oct 2018 14:20:02 -0400
To: Bresnitz, Eddy A.
Subject: Re: Adenovirus outbreak

Thanks. I am sending the info through that chain. Appreciate your help.

> On Oct 24, 2018, at 2:12 PM, Bresnitz, Eddy A. (b)(6) wrote:
>
>
> Nancy, NJ would like the name of the congressman and the health commissioner will reach out to him/her directly. FYI, apparently the governor is planning to hold a press conference this afternoon with the health commissioner about this outbreak. Eddy
>
> Sent from my iPhone
> Notice: This e-mail message, together with any attachments, contains
> information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth,
> New Jersey, USA 07033), and/or its affiliates Direct contact information
> for affiliates is available at
> <http://www.merck.com/contact/contacts.html> that may be confidential,
> proprietary copyrighted and/or legally privileged. It is intended solely
> for the use of the individual or entity named on this message. If you are
> not the intended recipient, and have received this message in error,
> please notify us immediately by reply e-mail and then delete it from
> your system.
>

From: Messonnier, Nancy (CDC/DDID/NCIRD/OD)
Sent: Fri, 14 Aug 2020 15:00:44 +0000
To: Ritchey, Julian /US
Cc: Melinda Wharton - CDC (mew2@cdc.gov)
Subject: RE: Updated State Claims Data

Thank you. We definitely appreciate having an independent data source on this. The public sector data seems to have more of a sense that many states are starting to catch up.

From: Ritchey, Julian /US <(b)(6)>
Sent: Thursday, August 13, 2020 3:53 PM
To: Wharton, Melinda (CDC/DDID/NCIRD/ISD) <mew2@cdc.gov>; Santoli, Jeanne (CDC/DDID/NCIRD/ISD) <zmd4@cdc.gov>; Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>
Cc: Binder, Tami /US <(b)(6)>
Subject: RE: Updated State Claims Data

They have been exceptional in all the data pulls I've seen.
They seem to have had an exuberant push...perhaps due to Dr. Feldman (a character if you know him!)

From: "mew2@cdc.gov" <mew2@cdc.gov>
Date: Thursday, August 13, 2020 at 3:48 PM
To: "Ritchey, Julian /US" <(b)(6)>, Jeanne Santoli <zmd4@cdc.gov>, "nar5@cdc.gov" <nar5@cdc.gov>
Cc: "Binder, Tami /US" <(b)(6)>
Subject: [EXTERNAL] RE: Updated State Claims Data

EXTERNAL : Real sender is mew2@cdc.gov

Thanks so much. Mississippi must have managed a robust back to school effort!

From: Ritchey, Julian /US <(b)(6)>
Sent: Thursday, August 13, 2020 3:38 PM
To: Santoli, Jeanne (CDC/DDID/NCIRD/ISD) <zmd4@cdc.gov>; Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>; Wharton, Melinda (CDC/DDID/NCIRD/ISD) <mew2@cdc.gov>
Cc: Binder, Tami /US <(b)(6)>
Subject: Updated State Claims Data

Dears –
Sharing revised claims data as previously discussed.

Unfortunately, I don't see a large positive movement in the overall data based on the summary slide of ped vs adult sales, but anecdotally, the pediatric providers are certainly trying.

Please let me know if this continues to be useful for you as well as any questions or suggestions. As always regarding this - and any messaging which we could amplify - we would be very interested in more granular conversations between our subject matter experts while there is still time to shape messaging, particularly flu.

I welcome your feedback and thoughts –
Julian

From: Messonnier, Nancy (CDC/DDID/NCIRD/OD)
Sent: Wed, 26 Aug 2020 14:14:56 +0000
To: (b)(6)
Subject: RE: chat

It would be good to catch up again
Nancy

From: Messonnier, Nancy (CDC/DDID/NCIRD/OD)
Sent: Tuesday, May 5, 2020 1:33 PM
To: (b)(6)
Subject: chat

Let me know if you have a few minutes to talk about COVID vaccines.
Nancy

From: Messonnier, Nancy (CDC/OID/NCIRD)
Sent: Thu, 8 Feb 2018 22:10:09 +0000
To: Ogden, Lydia
Subject: Re: Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018
Attachments: image001.jpg, image002.png, image004.png, image005.png, image006.png, image007.jpg

Thanks.

On Feb 8, 2018, at 4:42 PM, Ogden, Lydia <(b)(6)> wrote:

Dear CDC and Emory Colleagues: Thanks for including Julie in this exciting program. Please feel free to reach to me with any suggestions about key messages you'd like her to deliver or to coordinate with other panelists, etc. All the best. Y'all have been in our thoughts. LO

Lydia L. Ogden, PhD, MPP
Associate Vice President Global Enterprise Policy
Merck
Voice and text: (b)(6)
Email: (b)(6)
Executive Assistant: Jackie Cochran
Email: (b)(6)
Voice: (b)(6)
Desk: (b)(6)
<image001.jpg>
<image002.png> <image004.png>
<image005.png> <image006.png>

From: Krmpotich, Jane C
Sent: Thursday, February 08, 2018 4:33 PM
To: Sterk, Nancy
Cc: Painter, Elizabeth (CDC/OID/NCIRD) (CTR); Ogden, Lydia; Messonnier, Nancy (CDC/OID/NCIRD); Cozart, Barbara (CDC/OID/NCIRD)
Subject: RE: Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018

Hi Nancy and Dr. Painter,

I am pleased to let you know that Dr. Julie Gerberding looks forward to participating in this program on May 7 in Atlanta. I've noted the details on her calendar and will look for additional information regarding the event as the date approaches. Thank you.

Best regards,
Jane

Jane Krmpotich

Office of Julie L. Gerberding, M.D., M.P.H.

Executive Vice President & Chief Patient Officer

Strategic Communications, Global Public Policy, and Population Health

Merck & Co., Inc. | 351 N. Sumneytown Pike (UG4CD-04), North Wales, PA 19454 | Phone: (b)(6)

(b)(6)

[<image007.jpg>](#)

From: Sterk, Nancy [<mailto:nsterk@emory.edu>]

Sent: Monday, February 05, 2018 1:42 PM

To: Gerberding, Julie

Cc: Painter, Elizabeth (CDC/OID/NCIRD) (CTR); Krmpotich, Jane C; Ogden, Lydia

Subject: Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018"

EXTERNAL EMAIL – Use caution with any links or file attachments.

Good afternoon - I'm writing on behalf of Dr. Jim Curran to invite you to participate in the "100 years of Influenza Pandemics and Practice: 1918-2018" one-day symposium on Monday, May 7, 2018 in Atlanta, GA. The event is a partnership between the Rollins School of Public Health and the Centers for Disease Control and Prevention.

Attached to this email is the letter of invitation from Dr. Curran. Please respond directly to Dr. Eli Painter (copied on this email) with your availability.

We look forward to hearing back from you.

Nancy

Nancy Sterk

Executive Administrative Assistant to James W. Curran, MD, MPH / James W. Curran Dean of Public Health / Rollins School of Public Health, Emory University / 1518 Clifton Road, NE, Suite 8000E / Mailstop:1518-002-8BB / Atlanta, GA 30322 PH: (b)(6)

CELL: (b)(6) / FAX:404.712.8879 / email: nsterk@emory.edu / web:

<http://www.sph.emory.edu>

This e-mail message (including any attachments) is for the sole use of the intended recipient(s) and may contain confidential and privileged information. If the reader of this message is not the intended recipient, you are hereby notified that any dissemination, distribution or copying of this message (including any attachments) is strictly prohibited.

If you have received this message in error, please contact the sender by reply e-mail message and destroy all copies of the original message (including attachments).

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.





MERCK

INVENTING FOR LIFE











MERCK

INVENTING FOR LIFE

From: Messonnier, Nancy (CDC/OID/NCIRD)
Sent: Tue, 14 Apr 2015 13:40:35 +0000
To: York, Laura
Subject: Re: process question

Sure but am at coid so need to do it during the break

On Apr 14, 2015, at 8:15 AM, York, Laura <(b)(6)> wrote:

Hi Nancy

Would you have time to chat for 15 minutes this afternoon? I've an ACIP process question.

Thanks

Laura

Laura J. York, PhD

VP, Global Meningococcal Vaccines,
Medical Development and Scientific/Clinical Affairs

500 Arcola Road, Collegeville, PA, USA 19426
Vaccines | Pfizer Inc.

(b)(6)

From: Messonnier, Nancy (CDC/OID/NCIRD)
Sent: Thu, 18 Jun 2015 19:13:19 +0000
To: York, Laura
Subject: Re: know that you are busy with MERS but...

New enforcement of a rule - if a person comes to CDC more than 5 days/year they're supposed to have fingerprints and a badge. Most ACIP regulars come 6 days/year and have this requirement waived, but for some people who come more often, apparently, they want to enforce.

Cindy is seeing what she can do.

On Jun 18, 2015, at 3:03 PM, York, Laura <(b)(6)> wrote:

Thanks!

From: Messonnier, Nancy (CDC/OID/NCIRD) [<mailto:nar5@cdc.gov>]
Sent: Thursday, June 18, 2015 2:54 PM
To: Weinbaum, Cindy (CDC/OID/NCEZID)
Cc: York, Laura
Subject: FW: know that you are busy with MERS but...

Cindy,
Laura York regularly attends ACIP so I'm not sure why this is now a problem. We would obviously want her to attend ACIP. Can you try to resolve it? Note that Laura is a Canadian, not US citizen.
Thank you,

Nancy

From: York, Laura [[\(b\)\(6\)](mailto:(b)(6))]
Sent: Thursday, June 18, 2015 2:50 PM
To: Messonnier, Nancy (CDC/OID/NCIRD)
Subject: know that you are busy with MERS but...

Hey there. I am having an issue with getting security clearance for the ACIP meeting. Security is asking for fingerprints... I need a CDC number, as if I am working at CDC - and this too is a "lengthy process"....
Seriously? (one Security lady on the deck greets me by name!)
Any thoughts?

From: Messonnier, Nancy (CDC/OID/NCIRD)
Sent: Mon, 14 Mar 2016 15:39:51 +0000
To: York, Laura
Subject: Re: okay - now I can say Congrats!! (?)

Thank you.

On Mar 14, 2016, at 11:18 AM, York, Laura (b)(6) wrote:

Hi Nancy

I just received a note saying that you had accepted the position of Director, NCIRD as of April 4th. Now that it is official, my sincere congratulations. You deserve the recognition!

Warm regards

Laura

Laura J. York, PhD

VP, Global Meningococcal Vaccines,
Medical Development and Scientific/Clinical Affairs

500 Arcola Road, Collegeville, PA, USA 19426
Vaccines | Pfizer Inc.

(b)(6)

From: Messonnier, Nancy (CDC/OID/NCIRD)
Sent: Mon, 2 May 2016 13:32:46 +0000
To: Leonard Friedland
Cc: Cozart, Barbara (CDC/OID/NCIRD)
Subject: Re: GSK would like to discuss communication plans for influenza vaccine in infants with CDC

Ok. I'll also be at the first day of the NAHIS meeting next week.

> On May 2, 2016, at 9:23 AM, Leonard Friedland <(b)(6)> wrote:

>

> Of course. I will coordinate separately with Barbara in order to respect your email inbox

> Looking forward to speaking later this week

> Len

>

>> On May 2, 2016, at 8:28 AM, Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov> wrote:

>>

>> Sure. Happy to. Would Thursday or Friday work? I am cc'ing my Admin assistant, Barbara, to coordinate.

>>

>>> On May 2, 2016, at 7:43 AM, Leonard Friedland <(b)(6)> wrote:

>>>

>>> Dear Nancy,

>>> If you have a few minutes free sometime this week I would like to speak with you to discuss GSK and CDC beginning a dialog to plan for communications in anticipation of the (b)(4)

(b)(4) I ask to speak with you by phone as my colleague Catia Ferreira is waiting to hear back from Lisa Grohskopf.

>>> Please let me know when there is a good time to speak by phone for a few minutes this week.

>>> Best regards, Len

>>> (b)(6)

>>>

>>>

>>> -----Original Message-----

>>> From: Leonard Friedland

>>> Sent: Monday, April 18, 2016 7:52 AM

>>> To: Grohskopf Lisa; chw4@cdc.gov

>>> Cc: Catia Ferreira; Messonnier Nancy

>>> Subject: GSK would like to discuss communication plans for influenza vaccine in infants with CDC

>>>

>>> Dear Dr Grohskopf, Weinbaum and Messonnier,

>>>

>>> I am following up on the March 8 meeting where GSK discussed our vaccines pipeline with CDC. (b)(4)

(b)(4)

The expectation from the March 8 meeting was that GSK and CDC would begin such discussion within 30 days. As that time has passed, on behalf of my colleague Catia Ferreira please schedule with Catia time to begin these discussions. GSK wishes to share our communication plans and be aligned and coordinated with CDC.

>>> Thank you and best regards, Len

>>>

>>> Leonard Friedland, MD Vice President, Director Scientific Affairs and Public Health, Vaccines, North America
GlaxoSmithKline

>

From: Messonnier, Nancy (CDC/OID/NCIRD)
Sent: Mon, 18 Apr 2016 11:32:50 +0000
To: York, Laura
Subject: Re: Trumenba FDA Approval of Label Change

Thanks

On Apr 17, 2016, at 5:27 PM, York, Laura (b)(6) wrote:

Dear Nancy

Just a note to let you know that on Thursday, April 14, Pfizer received FDA approval to include the two-dose schedule, as well as the modification of the 3-dose schedule, in the Trumenba US label.

The approval letter and the label can be found on the FDA website using this link:
<http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm421020.htm>

If you've any questions, I'd be happy to speak with you.

Kind regards
Laura

Laura J. York, PhD
VP, Global Meningococcal Vaccines,
Medical Development and Scientific/Clinical Affairs

500 Arcola Road, Collegeville, PA, USA 19426
Vaccines | Pfizer Inc.

(b)(6)

From: Messonnier, Nancy (CDC/OID/NCIRD)
Sent: Wed, 7 Sep 2016 17:01:15 +0000
To: Grabenstein, John D.
Cc: Mitchell, Emily (CDC cdcfoundation.org)
Subject: Re: Information for Hilleman remarks
Attachments: image001.jpg, image002.jpg, image003.jpg, image004.jpg

I'd be happy to. I would need her bio.

On Sep 7, 2016, at 12:56 PM, Grabenstein, John D. <[REDACTED]> wrote:

Emily, here is the current version of my remarks for Tuesday evening. I may tinker with precise wording, but this gives you a sense of what I have in mind.

I assumed that Nancy would be giving particulars from Carol's CV (titles and positions and so forth), so I stayed away from them.

Happy to take any suggestions or feedback.

See you soon.

John

From: Mitchell, Emily [<mailto:emitchell@cdcfoundation.org>]
Sent: Tuesday, September 06, 2016 09:58
To: Grabenstein, John D.
Subject: RE: Information for Hilleman remarks

Thanks, John. I think that would be easiest. And you're alright with that brief intro of Dr. Messonnier as well?

Additionally, is this listing okay for the lecture programs? If not, please let me know what changes or additions I can make.

Opening Remarks

John Grabenstein, Ph.D., COL, USA (Ret.)
Executive Director, Global Health & Medical Affairs
Merck Vaccines
Merck & Co., Inc.

Thanks and happy Tuesday!

Emily Mitchell, Manager of Stewardship
CDC Foundation | 404.523.1873 | www.cdcfoundation.org

[<image001.jpg>](#) [<image002.jpg>](#) [<image003.jpg>](#) [<image004.jpg>](#)

Building innovative partnerships to advance
CDC's work to protect America and the world

From: Grabenstein, John D. [<mailto:john.d.grabenstein@cdc.gov>] (b)(6)
Sent: Sunday, September 04, 2016 6:13 PM
To: Mitchell, Emily <emitchell@cdcfoundation.org>
Subject: RE: Information for Hilleman remarks

I'm happy to introduce myself. No worries there. Whatever flows most smoothly.

John

From: Mitchell, Emily [<mailto:emitchell@cdcfoundation.org>]
Sent: Thursday, September 01, 2016 15:35
To: Grabenstein, John D.
Subject: RE: Information for Hilleman remarks

Hi again, John.

I hope you're gearing up for a relaxing holiday weekend!

I am thinking through the logistics of the run of show for remarks before the Hilleman Lecture. Since you are speaking directly after the film clip, is it okay with you if you introduce yourself? Or if you prefer, I could have Dr. Monroe stay at the podium through the film clip and introduce you when it's ended... Let me know which is better. I think either way would be fine.

Then, at the end of your remarks, would you please be so kind as to briefly introduce Dr. Messonnier, who speaks right after you? Something like, "Now, I'd like to welcome to the podium, Dr. Nancy Messonnier, director of CDC's National Center for Immunization and Respiratory Diseases, to introduce this evening's lecturer."

Thanks!
Emily

Emily Mitchell, Manager of Stewardship
CDC Foundation | 404.523.1873 | www.cdcfoundation.org

[<image001.jpg>](#) [<image002.jpg>](#) [<image003.jpg>](#) [<image004.jpg>](#)

Building innovative partnerships to advance
CDC's work to protect America and the world

From: Grabenstein, John D. [mailto: (b)(6)]
Sent: Friday, August 19, 2016 11:18 AM
To: Mitchell, Emily <emitchell@cdcfoundation.org>
Subject: RE: Information for Hilleman remarks

Simply perfect.

From: Mitchell, Emily [mailto:emitchell@cdcfoundation.org]
Sent: Friday, August 19, 2016 11:01
To: Grabenstein, John D.
Subject: RE: Information for Hilleman remarks

Hi John,

Thanks! Here is the link and password the film clip. Please let me know what you think!

(b)(6)
Password (case-sensitive): (b)(6)

Happy Friday!
Emily

Emily Mitchell, Manager of Stewardship
CDC Foundation | 404.523.1873 | www.cdcfoundation.org

<[image001.jpg](#)>
<[image002.jpg](#)> <[image003.jpg](#)> <[image004.jpg](#)>

Building innovative partnerships to advance
CDC's work to protect America and the world

From: Grabenstein, John D. [mailto: (b)(6)]
Sent: Friday, August 19, 2016 10:59 AM
To: Mitchell, Emily <emitchell@cdcfoundation.org>
Subject: RE: Information for Hilleman remarks

Emily, thanks for the bio.

I was going to work in the explanation of the Jeryl Lynn connection if there was no film clip, so I'm happy to have that accomplished in that way.

Things are looking good.

John

From: Mitchell, Emily [mailto:emitchell@cdcfoundation.org]
Sent: Thursday, August 18, 2016 14:35

To: Grabenstein, John D.

Subject: Information for Hilleman remarks

Hi John,

Hope you are well. I'm touching base to pass along some information that may be helpful to you as you are writing the introductory remarks for next month's Hilleman Lecture.

You may recall that I was exploring the idea of screening a portion of the documentary about Maurice Hilleman during the opening portion of the lecture. I think we will move forward with that idea and show approximately 3 minutes of the film—after opening remarks by our CEO Judy Monroe and before your introductory remarks. Does that sound okay to you?

The part of the film of interest explains Dr. Hilleman's development of the mumps vaccine (while he was working for Merck, I believe) and why it was named the Jeryl Lynn strain. If you're agreeable, I think it would be great if you could include some reference to the film in your remarks. The filmmaker will be sending me the three-minute clip soon—which I will forward along to you.

Additionally, I have attached Dr. Baker's bio for your reference.

Let me know if you have feedback, concerns or questions at all. Looking forward to hearing your thoughts.

Thanks,
Emily

Emily Mitchell, Manager of Stewardship

CDC Foundation | 404.523.1873 | www.cdcfoundation.org

<image001.jpg>

<image002.jpg> <image003.jpg> <image004.jpg>

Building innovative partnerships to advance
CDC's work to protect America and the world

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

<Hilleman Lecture 2016 Baker - Grabenstein .docx>











From: Messonnier, Nancy (CDC/DDID/NCIRD/OD)
Sent: Fri, 6 Sep 2019 19:10:25 +0000
To: Jodar, Luis
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD); Cane, Alejandro; Cocero, Nanette
Subject: RE: Re-defining the contacts between Pfizer medical and CDC

Luis,

Thank you for the email. I am also committed to trying to improve the relationships and appreciate your update around staff changes. Barb will work with Amanda around discussions with Alejandro and Vincenzo and I look forward to meeting Nanette at a future date. I will be meeting with Lisa Coen and David Hering at a Bio meeting next month.

Best,
Nancy

From: Jodar, Luis (b)(6)
Sent: Tuesday, September 3, 2019 10:35 AM
To: Messonnier, Nancy (CDC/DDID/NCIRD/OD) <narS@cdc.gov>
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>; Cane, Alejandro (b)(6); Cocero, Nanette (b)(6)
Subject: Re-defining the contacts between Pfizer medical and CDC

Dear Nancy,

I hope this email finds you well and you have had a great labor day week-end.

I am writing to you to inform you about a few changes in the Pfizer Vaccines Medical and Scientific organization with the aim at optimizing and streamlining the relationships between Pfizer vaccines medical and CDC colleagues.

Alejandro Cane has been appointed the new US Vaccines Medical and Scientific Affairs Lead replacing Raul Isturiz and reporting to me. He will be the primary contact to all things related to ACIP, and will liaise directly with both Amanda Cohn and Barbara Mahon.

For the specific vaccines working groups the point of contact for general communications will be Vincenzo Snow, supported by Pfizer subject matter experts from different vaccines.

On a related topic, we have a new Global President, Nanette Cocero, and we would be delighted to meet with you in person at your convenience to discuss areas of mutual interest.

I will always be at your disposal should any communications between you and I were needed.

Best regards,

Luis

Dr. Luis Jodar
Chief Medical and Scientific Affairs Officer, Vaccines
Pfizer Inc.

From: Messonnier, Nancy (CDC/DDID/NCIRD/OD)
Sent: Tue, 12 Nov 2019 00:28:27 +0000
To: Grabenstein, John D.
Subject: Re: European registration of Merck V920 Ebola vaccine

Congratulations and thanks for the heads up.

From: Grabenstein, John D. <(b)(6)>
Sent: Monday, November 11, 2019 7:26:08 PM
To: Choi, Mary Joung (CDC/DDID/NCEZID/DHCPP) <whz2@cdc.gov>; Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>
Cc: Collier, Beth-Ann Griswold <(b)(6)> Macareo, Louis Robert <(b)(6)>; Wolf, Jayanth <(b)(6)> Shah, Anant C <(b)(6)> Soloski, Drew <(b)(6)>
Subject: European registration of Merck V920 Ebola vaccine

Dr. Messonnier, CAPT Cohn, Dr. Choi,

This is a courtesy message to alert you that the European Medicines Agency (EMA) today granted registration to Merck's Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live), also known as V920 and now 'Ervebo.' EMA reviewed this vaccine under EMA's [accelerated assessment](#) program and it was granted conditional marketing authorization within the EU.

Please allow me to emphasize that this European decision has no bearing on the US status or availability of V920, insofar as the US Food & Drug Administration (FDA) has not yet reached a decision about V920. V920 remains an Investigational New Drug (IND) within the USA.

This EMA website reports the product in its CHMP-recommended status of mid-October 2019. The site will change shortly, we expect.

<https://www.ema.europa.eu/en/medicines/human/summaries-opinion/ervebo>.

I have attached the European Summary of Product Characteristics (SmPC), for your background information. This document or a similar version will appear at the EMA website in coming days. We would expect any language that FDA might approve sometime in the future to be different, to some greater or lesser extent that we cannot currently anticipate. We make no promise about what future action, if any, FDA may take.

Best regards, John

John D. Grabenstein, RPh, PhD
Executive Director, Global Medical Affairs -- Vaccines
Merck Research Laboratories
351 N. Sumneytown Pike, UG-2B09
North Wales, PA 19454-2505

www.MerckVaccines.com

desk

(b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

From: Messonnier, Nancy (CDC/DDID/NCIRD/OD)
Sent: Fri, 25 Oct 2019 17:14:33 +0000
To: Coen, Lisa
Subject: RE: Thank you

I really appreciate you taking the time but also your willingness to 'reset' the relationships.
Nancy

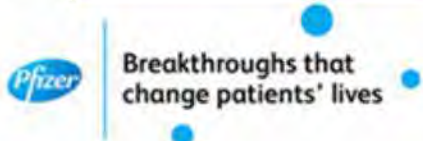
From: Coen, Lisa (b)(6)
Sent: Friday, October 25, 2019 8:46 AM
To: Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>; Aleshire, Noah (CDC/DDID/NCIRD/OD) <uwo2@cdc.gov>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD) <aji8@cdc.gov>; Mahon, Barbara (CDC/DDID/NCIRD/DBD) <bdm3@cdc.gov>
Cc: Hering, David (b)(6); Forte, Caroline (b)(6) Snow, Vincenza T (b)(6) Cane, Alejandro (b)(6)
Subject: Thank you

Dear Nancy, Amanda and team – on behalf of my colleagues, thank you for meeting with us yesterday and being so generous with your time during such a busy week for you. We appreciated the opportunity to have a candid and open discussion on improving our working relationship with you and your team members.

We're looking forward to working together going forward and will be circling back soon with Noah and Barbara on next steps. Thank you again.

Kind regards,
Lisa

~~~~~  
**Lisa Coen**  
U.S. Public Affairs | Pfizer Vaccines  
1275 Pennsylvania Ave, NW #600 | Washington, DC 20004  
Mobile: (b)(6)  
Email: (b)(6)





**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Sent:** Thu, 2 Jan 2020 17:32:09 +0000  
**To:** Ritchey, Julian /US  
**Cc:** Cohn, Amanda (CDC/DDID/NCIRD/OD); Grohskopf, Lisa A. (CDC/DDID/NCIRD/ID); Pope, Kristin (CDC/DDID/NCIRD/OD)  
**Subject:** RE: Influenza EO outreach  
**Attachments:** Thompson\_Comparative Immunogenicity.pdf

Thanks Julian.

The study (attached) came out before the holidays and am happy to be able to share it.

Happy New Year,

Nancy

**From:** Ritchey, Julian /US (b)(6)  
**Sent:** Wednesday, January 1, 2020 11:17 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Cc:** Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>; Grohskopf, Lisa A. (CDC/DDID/NCIRD/ID) <lkg6@cdc.gov>; Pope, Kristin (CDC/DDID/NCIRD/OD) <kfp7@cdc.gov>  
**Subject:** RE: Influenza EO outreach

Nancy –

I hope this finds you well and having enjoyed some downtime at the end of the year.

Following up on our pre-holiday call with Dr. Redfield. It was reassuring to hear thoughts from both of you on the meaning and course of the EO. Please count on us to help in any way we can to maximize the benefits and progress toward new technology while meeting the needs that our current vaccine options can provide....and provide to many more people than who take advantage of them today.

Your comment during the conversation regarding the CID study was noted and appreciated by myself and my team. We have since seen that data and are heartened by these early findings and their support for continued innovation. Would it be possible to connect with members of your team to discuss these results and how you anticipate messaging around them as these are important data for product development decision-making?

Thank you again -  
Julian

**From:** "nar5@cdc.gov" <nar5@cdc.gov>  
**Date:** Friday, December 6, 2019 at 10:21 AM  
**To:** "Ritchey, Julian /US" (b)(6)  
**Cc:** Amanda Cohn <anc0@cdc.gov>, Lisa Grohskopf <lkg6@cdc.gov>, Kristin Pope <kfp7@cdc.gov>  
**Subject:** [EXTERNAL] RE: Influenza EO outreach

**EXTERNAL :** Real sender is [nar5@cdc.gov](mailto:nar5@cdc.gov)

Julian

I appreciate the information and copy of the letter. We'll look forward to talking to you on Monday,  
Nancy

**From:** Ritchey, Julian /US (b)(6)  
**Sent:** Thursday, December 5, 2019 4:44 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <[anc0@cdc.gov](mailto:anc0@cdc.gov)>; Grohskopf, Lisa A. (CDC/DDID/NCIRD/ID) <[lkg6@cdc.gov](mailto:lkg6@cdc.gov)>; Pope, Kristin (CDC/DDID/NCIRD/OD) <[kfp7@cdc.gov](mailto:kfp7@cdc.gov)>  
**Subject:** Influenza EO outreach

Dear Nancy, et al.

I am reaching out to share a letter we recently sent to Dr. Kadlec to express our support, concerns, and suggestions related to the White House Influenza EO. As follow-up to this communication, we have been reaching out to Task Force stakeholders to share and discuss these thoughts.

We have secured time with Dr Redfield next Tuesday to discuss CDC engagement broadly and I see on the latest planner you have been included. I wanted to both share the context of the meeting and offer to discuss this as a separate group more specific to the key role we hope ACIP will be recognized as playing in any influenza policymaking especially as it regards impacts on seasonal immunization.

The letter is being shared with Dr. Redfield's office shortly as a pre-read for the call. Please let me know if you would be interested in discussing further.

Be well –  
Julian

# Comparative Immunogenicity of Several Enhanced Influenza Vaccine Options for Older Adults: A Randomized, Controlled Trial

Benjamin J. Cowling,<sup>1,\*</sup> Ranawaka A. P. M. Perera,<sup>1</sup> Sophie A. Valkenburg,<sup>1,2</sup> Nancy H. L. Leung,<sup>1</sup> A. Danielle Iuliano,<sup>3</sup> Yat Hung Tam,<sup>1</sup> Jennifer H. F. Wong,<sup>1</sup> Vicky J. Fang,<sup>1</sup> Athena P. Y. Li,<sup>1,2</sup> Hau Chi So,<sup>1</sup> Dennis K. M. Ip,<sup>1</sup> Eduardo Azziz-Baumgartner,<sup>3</sup> Alicia M. Fry,<sup>3</sup> Min Z. Levine,<sup>3</sup> Shivaprakash Gangappa,<sup>3</sup> Suryaprakash Sambhara,<sup>3</sup> Ian G. Barr,<sup>4,5</sup> Danuta M. Skowronski,<sup>6,7</sup> J. S. Malik Peiris,<sup>1</sup> and Mark G. Thompson<sup>3</sup>

<sup>1</sup>World Health Organization Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, The University of Hong Kong, Hong Kong Special Administrative Region, Hong Kong, China, <sup>2</sup>The University of Hong Kong-Pasteur Research Pole, School of Public Health, The University of Hong Kong, Hong Kong Special Administrative Region, Hong Kong, China, <sup>3</sup>Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, <sup>4</sup>World Health Organization Collaborating Centre for Reference and Research, Melbourne, Victoria, Australia, <sup>5</sup>Department of Microbiology and Immunology, University of Melbourne, Victoria, Australia, <sup>6</sup>British Columbia Centre for Disease Control, Vancouver, Canada, and <sup>7</sup>University of British Columbia, Vancouver, Canada

**Background.** Enhanced influenza vaccines may improve protection for older adults, but comparative immunogenicity data are limited. Our objective was to examine immune responses to enhanced influenza vaccines, compared to standard-dose vaccines, in community-dwelling older adults.

**Methods.** Community-dwelling older adults aged 65–82 years in Hong Kong were randomly allocated (October 2017–January 2018) to receive 2017–2018 Northern hemisphere formulations of a standard-dose quadrivalent vaccine, MF59-adjuvanted trivalent vaccine, high-dose trivalent vaccine, or recombinant-hemagglutinin (rHA) quadrivalent vaccine. Sera collected from 200 recipients of each vaccine before and at 30-days postvaccination were assessed for antibodies to egg-propagated vaccine strains by hemagglutination inhibition (HAI) and to cell-propagated A/Hong Kong/4801/2014(H3N2) virus by microneutralization (MN). Influenza-specific CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses were assessed in 20 participants per group.

**Results.** Mean fold rises (MFR) in HAI titers to egg-propagated A(H1N1) and A(H3N2) and the MFR in MN to cell-propagated A(H3N2) were statistically significantly higher in the enhanced vaccine groups, compared to the standard-dose vaccine. The MFR in MN to cell-propagated A(H3N2) was highest among rHA recipients (4.7), followed by high-dose (3.4) and MF59-adjuvanted (2.9) recipients, compared to standard-dose recipients (2.3). Similarly, the ratio of postvaccination MN titers among rHA recipients to cell-propagated A(H3N2) recipients was 2.57-fold higher than the standard-dose vaccine, which was statistically higher than the high-dose (1.33-fold) and MF59-adjuvanted (1.43-fold) recipient ratios. Enhanced vaccines also resulted in the boosting of T-cell responses.

**Conclusions.** In this head-to-head comparison, older adults receiving enhanced vaccines showed improved humoral and cell-mediated immune responses, compared to standard-dose vaccine recipients.

**Clinical Trials Registration.** NCT03330132.

**Keywords.** influenza; vaccination; public health.

Influenza vaccination is the cornerstone public health intervention to reduce the annual burden of influenza epidemics [1]. The most widely used influenza vaccines are inactivated influenza vaccines, administered intramuscularly [2]. Trivalent inactivated influenza vaccines contain a total of 45 µg of hemagglutinin (HA), with a “standard dose” (SD) of 15 µg each of influenza A(H1N1), A(H3N2), and B strains, while quadrivalent

vaccines contain an additional 15 µg HA of a second B strain. While these are the most commonly used vaccines, their effectiveness is variable from year to year [3].

Enhanced influenza vaccines have the potential to overcome issues associated with an aging immune system and reduced vaccine effectiveness [4–7]. The MF59-adjuvanted vaccine (FluAD) includes MF59, a squalene-based emulsion, in addition to 45 µg of HA (trivalent formulation), and produces a stronger immune response than the SD vaccine [8, 9], including increased breadth, diversity, and avidity of HA antibodies [10]. However, there are no available trials comparing the clinical efficacy of the MF59-adjuvanted vaccine to the SD vaccine in older adults. The trivalent high-dose (HD) vaccine, FluZone, contains a total of 180 µg of HA (60 µg of each HA): that is, 4 times the antigen of a trivalent SD vaccine. Compared to an

Received 15 July 2019; editorial decision 10 October 2019; accepted 14 October 2019; published online December 12, 2019.

Correspondence: B. J. Cowling, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 7 Sassoon Road, Pokfulam, Hong Kong Special Administrative Region, China (bcowling@hku.hk).

**Clinical Infectious Diseases®** 2019;XX(X):1–11

Published by Oxford University Press for the Infectious Diseases Society of America 2019. This work is written by (a) US Government employee(s) and is in the public domain in the US.  
DOI: 10.1093/cid/ciz1034



SD vaccine, the IID vaccine induced significantly higher antibody responses [11] and provided better efficacy than the SD vaccine against laboratory-confirmed influenza among older adults [12]. A recombinant HA-protein quadrivalent influenza vaccine, FluBlok, includes 180 µg of HA (45 µg of each HA), produced by Baculovirus expression in insect SF9 cell culture [13, 14]. This vaccine was more efficacious than an SD vaccine in preventing polymerase chain reaction-confirmed influenza among adults aged ≥50 years [15].

Although there is some evidence to support improved protection among older adults for these 3 enhanced influenza vaccines, multiple knowledge gaps remain. The immunogenicity of enhanced vaccines has not been directly compared against the same influenza vaccine antigens within the same population. This is especially important for the A(H3N2) vaccine component, given the lower clinical effectiveness against A(H3N2) illness among older adults [16] and the effects of egg adaptations observed in association with A(H3N2) vaccine components [17]. Therefore, we conducted a randomized, controlled trial to examine immune responses to 3 enhanced influenza vaccines, compared to SD vaccines, in community-dwelling older adults. Because antibody responses have limitations as predictors of vaccine efficacy, especially among older adults [18], we also compared T-cell responses to the vaccines [19]. Although large vaccine efficacy trials will ultimately be needed to clarify the relative preventive benefits of enhanced vaccines among older adults, over the course of this immunogenicity trial we aim to directly quantify and compare relative differences in immune responses to inform this substantial future investment.

## METHODS

### Recruitment and Follow-up of Participants

We enrolled community-dwelling older adults who were: (1) 65–82 years of age; (2) residing in Hong Kong; and (3) had not already received the Northern hemisphere 2017–2018 formulation of the influenza vaccine. Minor exclusion criteria and details on recruitment methods are described in the [Supplementary Appendix](#).

Because we intend to examine alternative combinations of repeated vaccinations with SD and enhanced vaccines in future years of this trial, we randomized participants to 11 different groups (see the [Supplementary Appendix](#)). In Year 1, we randomized 3/11 (27%) participants to receive an SD quadrivalent vaccine (0.5 mL FluQuadri), 3/11 (27%) to receive a trivalent MF59-adjuvanted vaccine (0.5 mL FLUAD, Seqirus), 3/11 (27%) to receive a trivalent high-dose vaccine (0.5 mL Fluzone High-Dose, Sanofi Pasteur), and 2/11 (18%) to receive a quadrivalent recombinant-HA vaccine (0.5 mL Flublok, Sanofi Pasteur). All vaccines included the strains recommended for the Northern hemisphere 2017–2018 formulation: namely, the A/Michigan/45/2015(H1N1)-like virus (clade 6B.1), A/

Hong Kong/4801/2014(H3N2)-like virus (clade 3C.2a), and B/Brisbane/60/2008-like virus (Victoria lineage; clade 1A), and the quadrivalent vaccines also included the B/Phuket/3073/2013-like virus (Yamagata lineage; clade 3).

We used R software to generate a block-randomized allocation sequence (see the [Supplementary Appendix](#)), which was concealed from the study staff. Study vaccines were repackaged into numbered boxes, based on the allocation sequence, by a research assistant who had no contact with participants. The study was blinded to participants, researchers, and laboratory staff, but was not blinded to the nurse who removed the vaccine from the numbered box and administered it. Randomization was done immediately prior to the administration of the vaccine for each participant.

We collected a 9 mL blood sample from each participant immediately prior to vaccination and 30 days (range, 26–35 days) after vaccination. A nonrandom, voluntary subset of 10% of participants (see the [Supplementary Appendix](#)) was invited to provide an additional 10 mL of heparinized whole-blood specimens at baseline, 7 days, and 30 days after vaccination for the extraction of peripheral blood mononuclear cells (PBMCs) and testing for cell-mediated immune responses to vaccination.

After vaccination, participants were observed for 15 minutes for acute reactions, and contacted at 1, 3, 7, and 14 days after vaccination to record any adverse events. During the 30-day postvaccination visit, we collected information on any serious adverse events since vaccination.

### Ethics

Signed, informed consent was obtained from all participants. The study protocol was approved by the Institutional Review Board of the University of Hong Kong.

### Laboratory Methods

A subset of 200 pairs of Day 0 and Day 30 sera from each of the 4 vaccine groups were selected, including all sera from the participants in the nonrandom 10% subset who provided PBMCs, plus a random sample of the other participants (see the [Supplementary Appendix](#)). Sera were tested by hemagglutination inhibition (HAI) assays against egg-propagated vaccine strains A/Singapore/GP1908/2015 (A/Michigan/45/2015[H1N1]-like virus), A/Hong Kong/4801/2014(H3N2), B/Brisbane/60/2008, and B/Phuket/3073/2013. In addition, we tested the sera by virus microneutralization (MN) against cell-propagated virus, which is more similar to the circulating strains, failed to agglutinate red blood cells (see the [Supplementary Appendix](#)).

In a subset of 20 participants in each of the 4 vaccine groups, influenza-specific CD4<sup>+</sup> and CD8<sup>+</sup> T-cell responses against influenza A(H1N1), A(H3N2), and B vaccine strains were assessed by flow cytometry for interferon (IFN)- $\gamma$  production after in vitro stimulation (see the [Supplementary Appendix](#)) to determine

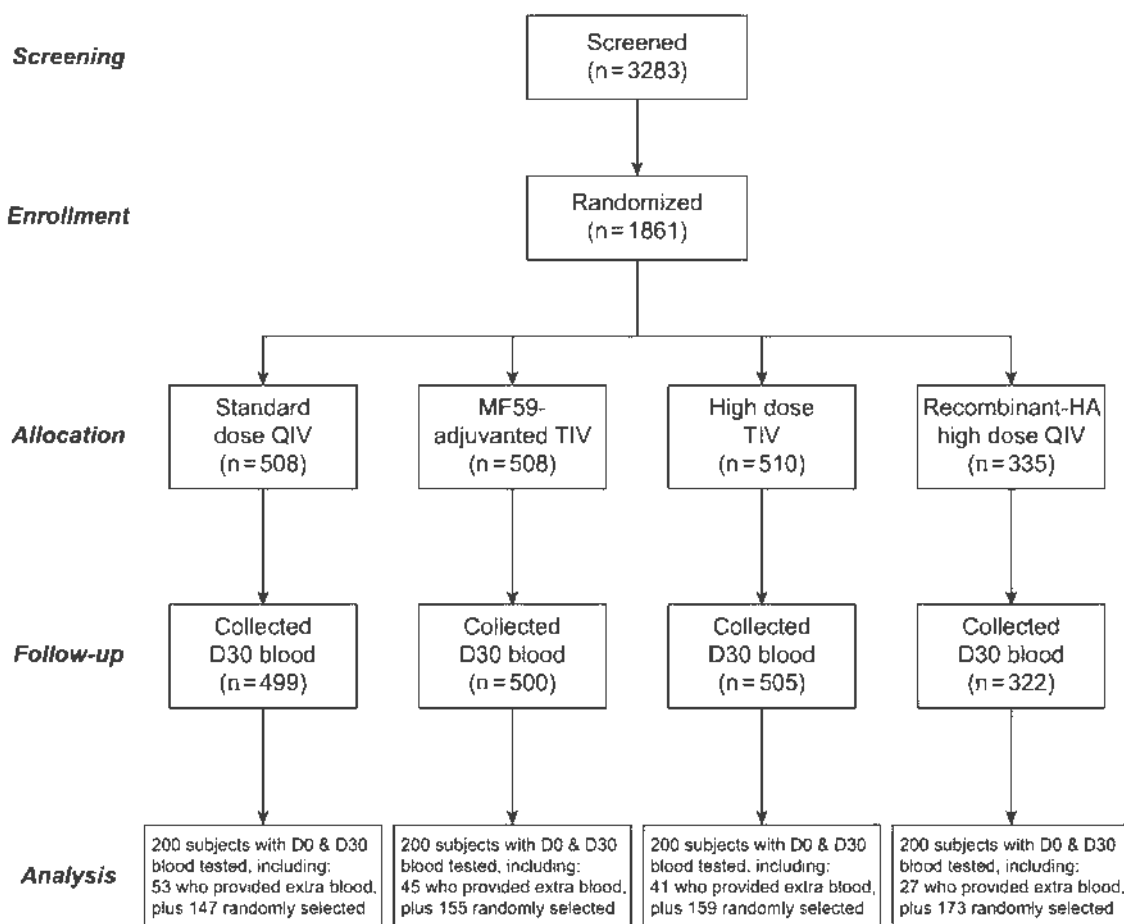
CD8<sup>+</sup> and CD4<sup>+</sup> T-cell recall responses at Day 7 and memory responses at Day 30, compared to prevaccination (Day 0) [20].

### Outcome Measures

Following the approach taken by a recent review of randomized trials comparing the immunogenicity of alternative influenza vaccine types among older adults [5], the primary outcome measures relate to the immune responses, measured by antibody titers against the vaccine strains in each enhanced vaccine group, compared to SD, including: (1) the proportion of participants who achieved a 4-fold or greater rise in postvaccination titers from Day 0 to Day 30 with a postvaccination titer  $\geq 40$ ; and (2) the geometric mean titer (GMT) at Day 30. In addition, we examined 3 protocol-specified secondary outcome measures: (1) the proportion of participants who achieved a postvaccination (Day 30) antibody titer  $\geq 40$  (and further elevated titers of  $\geq 80$  and  $\geq 160$ ); (2) the fold rise of vaccine-specific IFN- $\gamma$ <sup>+</sup> CD4<sup>+</sup> and IFN- $\gamma$ <sup>+</sup> CD8<sup>+</sup> T-cell responses at 7 (acute) and 30 (memory) days postvaccination, compared to prevaccination (Day 0); and (3) the rate of adverse events within 30 days after each vaccination.

### Statistical Analysis

We estimated the proportion of participants with a  $\geq 4$ -fold rise in antibody titers that led to a postvaccination titer  $\geq 40$ , the GMTs at Day 0 and Day 30, and the mean fold rise (MFR) from Day 0 to Day 30, with 95% confidence intervals. We calculated the ratio of postvaccination GMTs in each enhanced vaccine group, compared to the postvaccination GMT in the SD group, with 95% confidence intervals. We estimated the proportions of participants with postvaccination titers  $\geq 40$ ,  $\geq 80$ , and  $\geq 160$  in each vaccination group, and compared the proportions in the other 3 vaccination groups versus an SD quadrivalent influenza vaccine (QIV), using Chi-squared tests. Although *P* values  $< .05$  were considered statistically significant in order to optimize sensitivity to differences between exposure groups, we considered as noteworthy any patterns of effects that were repeated across outcomes. As previously noted [21], with a *P* value threshold  $< .05$ , a statistically significant difference can be observed even when 95% confidence intervals for the estimate overlap. All statistical analyses were conducted using R version 3.4.3.



**Figure 1.** Flow chart of participants through the study, and selection of 200 participants per group for serologic analysis. Abbreviations: D, day; HA, hemagglutinin; QIV, quadrivalent influenza vaccine; TIV, trivalent influenza vaccine.

### Sample Size Justification

For the present comparison of responses to 4 different vaccines in Year 1, we sought to detect small to moderate but meaningful relative differences in immunogenicity. A sample size of 200 participants per group would permit 80% power to detect increases of  $\geq 14\%$  in the proportion of enhanced vaccine recipients with  $\geq 4$ -fold rises in titer, and GMT ratios of 1.4 or higher in the enhanced vaccine groups, compared to a SD vaccine. Overall, we aimed to enroll 2200 participants into our study, anticipating a 10% dropout rate per year and a final sample size of at least 146 participants in each group through to the fourth year of the planned trial (see the [Supplementary Appendix](#)).

### RESULTS

We screened 3283 older adults, of whom 2695 were eligible and 2039 agreed to participate. We obtained signed informed consent from 2008 persons and were able to randomize and vaccinate 1861 participants from 7 October 2017 through 12 January 2018, of whom 1826 provided Day 30 postvaccination serum samples ([Figure 1](#)). About 10% of participants were asked to give additional blood; 168 contributed PBMCs for analyses of cell-mediated immunity.

Participants were balanced by age, sex, underlying medical conditions, and prior vaccination history between the 4 study groups, with no statistically significant differences in these key

variables overall or among those contributing to the primary antibody findings reported here ([Table 1](#)). The most common underlying conditions were hypertension, osteoarthritis, and diabetes. Most participants (66%) had received an influenza vaccination in the preceding year (2016–2017), and only 22% had not received any influenza vaccination in the preceding 5 years. All prior influenza vaccinations were with an SD vaccine. We selected 200 participants from each group for a serologic analysis, and the characteristics of this subset were representative of the entire cohort ([Table 2](#)). Pre- and post-vaccination GMTs and corresponding MFRs are described in [Table 3](#) for each vaccine group, and [Figure 2](#) presents comparisons of the MFRs between the enhanced vaccine groups and the SD group. [Table 4](#) shows the proportions of participants achieving specific titer thresholds after vaccination.

There were no statistically significant baseline differences between the groups in prevaccination GMTs for each of the antigens tested, except that the baseline GMTs to the B/Victoria antigen were statistically significantly lower in the SD group ([Table 3](#)). As shown in [Table 3](#), among SD QIV recipients, the HAI GMT to A(H1N1) increased from 17 to 69. MF59-adjuvanted and HD recipients achieved a significantly higher postvaccination GMT to A(H1N1) than SD recipients; recombinant-HA recipients did not. Nonetheless, MFRs for A(H1N1) were statistically significantly higher for all 3

**Table 1. Baseline Characteristics of the 1861 Participants, by Vaccination Group**

| Characteristics                                                                      | All Participants                            |       |                                            |       |                                      |       |                                              |       |
|--------------------------------------------------------------------------------------|---------------------------------------------|-------|--------------------------------------------|-------|--------------------------------------|-------|----------------------------------------------|-------|
|                                                                                      | Standard-dose quadrivalent vaccine, n = 508 |       | MF59-adjuvanted trivalent vaccine, n = 508 |       | High-dose trivalent vaccine, n = 510 |       | Recombinant-HA quadrivalent vaccine, n = 335 |       |
|                                                                                      | n                                           | (%)   | n                                          | (%)   | n                                    | (%)   | n                                            | (%)   |
| Age, years                                                                           |                                             |       |                                            |       |                                      |       |                                              |       |
| 65–70                                                                                | 269                                         | (53%) | 248                                        | (49%) | 258                                  | (51%) | 171                                          | (51%) |
| 71–76                                                                                | 130                                         | (26%) | 149                                        | (29%) | 143                                  | (28%) | 82                                           | (24%) |
| 77–82                                                                                | 109                                         | (21%) | 111                                        | (22%) | 109                                  | (21%) | 82                                           | (24%) |
| Female sex                                                                           | 301                                         | (59%) | 308                                        | (61%) | 327                                  | (64%) | 195                                          | (58%) |
| Underlying medical conditions                                                        |                                             |       |                                            |       |                                      |       |                                              |       |
| Hypertension                                                                         | 230                                         | (45%) | 262                                        | (52%) | 239                                  | (47%) | 161                                          | (48%) |
| Osteoarthritis                                                                       | 110                                         | (22%) | 102                                        | (20%) | 109                                  | (21%) | 70                                           | (21%) |
| Diabetes                                                                             | 98                                          | (19%) | 104                                        | (20%) | 88                                   | (17%) | 61                                           | (18%) |
| Heart diseases                                                                       | 52                                          | (10%) | 47                                         | (9%)  | 52                                   | (10%) | 29                                           | (9%)  |
| Cancer                                                                               | 46                                          | (9%)  | 43                                         | (8%)  | 40                                   | (8%)  | 22                                           | (7%)  |
| Others <sup>a</sup>                                                                  | 209                                         | (41%) | 221                                        | (44%) | 226                                  | (44%) | 141                                          | (42%) |
| Received influenza vaccination in 2016–2017 season                                   | 328                                         | (65%) | 332                                        | (65%) | 351                                  | (69%) | 226                                          | (67%) |
| Number of times received influenza vaccination in the preceding 5 years <sup>b</sup> |                                             |       |                                            |       |                                      |       |                                              |       |
| 0                                                                                    | 126                                         | (25%) | 104                                        | (20%) | 111                                  | (22%) | 71                                           | (21%) |
| 1–2                                                                                  | 113                                         | (22%) | 120                                        | (24%) | 112                                  | (22%) | 68                                           | (20%) |
| 3–4                                                                                  | 54                                          | (11%) | 45                                         | (9%)  | 61                                   | (12%) | 38                                           | (11%) |
| 5–6                                                                                  | 195                                         | (38%) | 201                                        | (40%) | 212                                  | (42%) | 144                                          | (43%) |

Abbreviation: HA, hemagglutinin.

<sup>a</sup>Other underlying conditions included: stroke, chronic lung disease, kidney disease, liver disease, depression or anxiety disorder, neurologic disorder, autoimmune disease, disease of the digestive system, hypothyroidism, dermatological disease, etc.

<sup>b</sup>There were 6 possible influenza vaccines, including the 5 Northern hemisphere influenza vaccines from 2012–2013 through 2016–2017 plus the Southern hemisphere 2015 vaccine, which was available in Hong Kong for a special vaccination campaign [20]. The Southern hemisphere formulation is not usually available in Hong Kong.



**Table 2. Baseline Characteristics of the Subset of 800 Participants Selected for Immunogenicity Analyses**

|                                                                                      | Participants Selected for Immunogenicity Analysis |       |                                            |       |                                      |       |                                              |       |
|--------------------------------------------------------------------------------------|---------------------------------------------------|-------|--------------------------------------------|-------|--------------------------------------|-------|----------------------------------------------|-------|
|                                                                                      | Standard-dose quadrivalent vaccine, n = 200       |       | MF59-adjuvanted trivalent vaccine, n = 200 |       | High-dose trivalent vaccine, n = 200 |       | Recombinant-HA quadrivalent vaccine, n = 200 |       |
|                                                                                      | n                                                 | (%)   | n                                          | (%)   | n                                    | (%)   | n                                            | (%)   |
| Age, years                                                                           |                                                   |       |                                            |       |                                      |       |                                              |       |
| 65–70                                                                                | 105                                               | (52%) | 96                                         | (48%) | 106                                  | (53%) | 101                                          | (50%) |
| 71–76                                                                                | 44                                                | (22%) | 59                                         | (30%) | 52                                   | (26%) | 53                                           | (26%) |
| 77–82                                                                                | 51                                                | (26%) | 45                                         | (22%) | 42                                   | (21%) | 46                                           | (23%) |
| Female sex                                                                           | 119                                               | (60%) | 119                                        | (60%) | 127                                  | (64%) | 120                                          | (60%) |
| Underlying medical conditions                                                        |                                                   |       |                                            |       |                                      |       |                                              |       |
| Hypertension                                                                         | 95                                                | (48%) | 105                                        | (52%) | 92                                   | (46%) | 101                                          | (50%) |
| Osteoarthritis                                                                       | 44                                                | (22%) | 36                                         | (18%) | 41                                   | (20%) | 49                                           | (24%) |
| Diabetes                                                                             | 43                                                | (22%) | 41                                         | (20%) | 38                                   | (19%) | 37                                           | (18%) |
| Heart diseases                                                                       | 22                                                | (11%) | 11                                         | (6%)  | 20                                   | (10%) | 21                                           | (10%) |
| Cancer                                                                               | 20                                                | (10%) | 14                                         | (7%)  | 15                                   | (8%)  | 15                                           | (8%)  |
| Others <sup>a</sup>                                                                  | 83                                                | (42%) | 81                                         | (40%) | 82                                   | (41%) | 89                                           | (44%) |
| Received influenza vaccination in 2016–2017 season                                   | 136                                               | (68%) | 130                                        | (65%) | 139                                  | (70%) | 137                                          | (69%) |
| Number of times received influenza vaccination in the preceding 5 years <sup>b</sup> |                                                   |       |                                            |       |                                      |       |                                              |       |
| 0                                                                                    | 46                                                | (23%) | 45                                         | (22%) | 46                                   | (23%) | 47                                           | (24%) |
| 1–2                                                                                  | 46                                                | (23%) | 43                                         | (22%) | 34                                   | (17%) | 41                                           | (20%) |
| 3–4                                                                                  | 29                                                | (14%) | 21                                         | (10%) | 26                                   | (13%) | 19                                           | (10%) |
| 5–6                                                                                  | 74                                                | (37%) | 78                                         | (39%) | 90                                   | (45%) | 87                                           | (44%) |

Abbreviation: HA, hemagglutinin.

<sup>a</sup>Other underlying conditions included: stroke, chronic lung disease, kidney disease, liver disease, depression or anxiety disorder, neurologic disorder, autoimmune disease, disease of the digestive system, hypothyroidism, dermatological disease, etc.<sup>b</sup>There were 6 possible influenza vaccines, including the 5 Northern hemisphere influenza vaccines from 2012–2013 through 2016–2017 plus the Southern hemisphere 2015 vaccine, which was available in Hong Kong for a special vaccination campaign [20]. The Southern hemisphere formulation is not usually available in Hong Kong.

enhanced vaccines (range, 5.3–6.1) compared to the SD (4.1; Table 3; Figure 2). The proportions with  $\geq 4$ -fold rises to titers  $\geq 40$  were statistically significantly higher for all 3 enhanced vaccines (range, 59–60%) compared to the SD QIV (42%). As shown in Table 4, the proportions achieving elevated titers of  $\geq 40$  were higher for the MF59-adjuvanted (82%) and HD (83%) groups, compared to the SD recipients (72%). Of note, the proportions achieving very high titers of  $\geq 160$  were significantly higher for all 3 enhanced vaccines (45–55%), compared to the SD vaccine (35%).

Recipients of all 3 enhanced vaccines achieved higher postvaccination GMTs and greater MFRs to both the egg-propagated A(H3N2) by HAI and the cell-propagated A(H3N2) by MN than recipients of SD vaccines (Table 3; Figure 2). The directions of the effects were similar using other indicators. Of note, only 28% of SD recipients achieved  $\geq 4$ -fold rises in MN responses to cell-propagated A(H3N2), compared to 39% of MF59-adjuvant, 47% of HD QIV, and 57% of recombinant-HA QIV recipients ( $P < .01$ ; Table 3).

On several indicators, antibody responses to cell-propagated A(H3N2) by MN were significantly higher among recombinant-HA QIV recipients, compared to SD vaccine, MF59-adjuvant, and HD recipients (Table 3). Specifically, recipients of recombinant-HA QIV achieved a postvaccination GMT to cell-propagated A(H3N2) that was 2.57-fold higher

than that of SD recipients; the magnitude of this difference was significantly higher than the 1.43- and 1.33-fold differences of MF59-adjuvanted and HD recipients, respectively, compared to SD recipients (Figure 2). Recombinant-HA recipients were the only enhanced vaccine group with a significantly larger proportion (74%) of very high titers ( $\geq 160$ ) against cell-propagated A(H3N2), compared to SD recipients (48%; Table 4).

Responses to the B/Victoria component of both the trivalent influenza vaccine (TIV) and QIV in the study year (B/Brisbane/60/2008) were similar across vaccines, with the exception of a significantly higher GMT of HD TIV, compared with SD QIV (Figure 2). Although the MFRs against B/Phuket/3073/2013 were statistically significantly  $> 1$  for both SD and enhanced vaccines (Table 3), the GMTs were significantly lower, compared with the SD QIV, for the MF-59-adjuvanted and HD TIVs, which did not include this B/Yamagata component (Figure 2). The response to recombinant-HA QIV that did include B/Yamagata was not significantly different to SD QIV on any indicator.

For T-cell responses at 7 and 30 days postvaccination, we noted a trend whereby enhanced influenza vaccines elicited increased peak acute IFN- $\gamma^+$  T-cell responses and maintained higher average memory responses for selected time points and viruses (Figure 3; Supplementary Appendix Table 5). For influenza-specific IFN- $\gamma^+$  CD8 $^+$  T-cell responses, statistically

**Table 3. Summary of Pre- and Post-vaccination Antibody Titers and Fold Rises in Each Vaccination Group**

| Assay | Strain                                             | Vaccination Group          |           |                              |           |                        |           |                             |           |
|-------|----------------------------------------------------|----------------------------|-----------|------------------------------|-----------|------------------------|-----------|-----------------------------|-----------|
|       |                                                    | Standard-dose QIV, n = 200 |           | MF59-adjuvanted TIV, n = 200 |           | High-dose TIV, n = 200 |           | Recombinant-HA QIV, n = 200 |           |
|       |                                                    | Estimate                   | (95% CI)  | Estimate                     | (95% CI)  | Estimate               | (95% CI)  | Estimate                    | (95% CI)  |
| HAI   | A/Michigan/45/2015 (H1N1)                          |                            |           |                              |           |                        |           |                             |           |
|       | Day 0 GMT                                          | 17                         | (14–20)   | 17                           | (15–20)   | 20                     | (17–24)   | 16                          | (14–19)   |
|       | Day 30 GMT                                         | 69                         | (58–83)   | 94*                          | (78–114)  | 125*                   | (102–152) | 85                          | (69–105)  |
|       | Mean fold rise from D0 to D30                      | 4.1                        | (3.5–4.9) | 5.5*                         | (4.6–6.6) | 6.1*                   | (5.1–7.3) | 5.3*                        | (4.4–6.3) |
|       | % with ≥4-fold rise from D0 to D30 <sup>b</sup>    | 42%                        | (36–50%)  | 60%*                         | (53–67%)  | 59%*                   | (52–66%)  | 60%*                        | (53–67%)  |
| HAI   | A/Hong Kong/4801/2014 (H3N2) egg-like              |                            |           |                              |           |                        |           |                             |           |
|       | Day 0 GMT                                          | 46                         | (39–56)   | 49                           | (41–59)   | 45                     | (38–54)   | 54                          | (45–64)   |
|       | Day 30 GMT                                         | 158                        | (135–186) | 207*                         | (178–241) | 214*                   | (183–250) | 254*                        | (218–295) |
|       | Mean fold rise from D0 to D30                      | 3.4                        | (2.8–4.1) | 4.2*                         | (3.5–5.1) | 4.7*                   | (3.9–5.7) | 4.7*                        | (3.9–5.7) |
|       | % with ≥4-fold rise from D0 to D30 <sup>a</sup>    | 41%                        | (34–48%)  | 48%                          | (40–55%)  | 54%*                   | (46–61%)  | 56%*                        | (48–63%)  |
| MN    | A/Hong Kong/4801/2014 (H3N2) cell-like             |                            |           |                              |           |                        |           |                             |           |
|       | Day 0 GMT                                          | 38                         | (31–46)   | 43                           | (35–53)   | 34                     | (28–41)   | 48                          | (39–59)   |
|       | Day 30 GMT                                         | 87                         | (72–106)  | 125*                         | (102–152) | 116*                   | (95–141)  | 223*                        | (189–263) |
|       | Mean fold rise from D0 to D30                      | 2.3                        | (2.0–2.6) | 2.9*                         | (2.5–3.4) | 3.4*                   | (2.9–4.0) | 4.7*                        | (3.9–5.6) |
|       | % with ≥4-fold rise from D0 to D30 <sup>a</sup>    | 28%                        | (22–35%)  | 39%*                         | (32–46%)  | 47%*                   | (40–54%)  | 57%*                        | (50–64%)  |
| HAI   | B/Brisbane/60/2008 (Victoria lineage)              |                            |           |                              |           |                        |           |                             |           |
|       | Day 0 GMT                                          | 24                         | (20–28)   | 31*                          | (26–38)   | 31*                    | (26–37)   | 29*                         | (25–35)   |
|       | Day 30 GMT                                         | 89                         | (75–105)  | 95                           | (81–112)  | 132*                   | (112–157) | 90                          | (76–107)  |
|       | Mean fold rise from D0 to D30                      | 3.7                        | (3.2–4.4) | 3.0                          | (2.6–3.5) | 4.2                    | (3.5–5.0) | 3.1                         | (2.7–3.5) |
|       | % with ≥4-fold rise from D0 to D30 <sup>a</sup>    | 48%                        | (41–56%)  | 44%                          | (37–51%)  | 52%                    | (45–60%)  | 44%                         | (37–51%)  |
| HAI   | B/Phuket/3073/2013 <sup>b</sup> (Yamagata lineage) |                            |           |                              |           |                        |           |                             |           |
|       | Day 0 GMT                                          | 37                         | (31–44)   | 41                           | (35–49)   | 41                     | (34–50)   | 45                          | (38–54)   |
|       | Day 30 GMT                                         | 121                        | (104–141) | 63*                          | (54–74)   | 68*                    | (57–81)   | 131                         | (111–155) |
|       | Mean fold rise from D0 to D30                      | 3.3                        | (2.8–3.8) | 1.5*                         | (1.4–1.7) | 1.6*                   | (1.5–1.8) | 2.9                         | (2.5–3.3) |
|       | % with ≥4-fold rise from D0 to D30 <sup>a</sup>    | 42%                        | (36–50%)  | 12%*                         | (8–18%)   | 15%*                   | (10–21%)  | 42%                         | (36–50%)  |

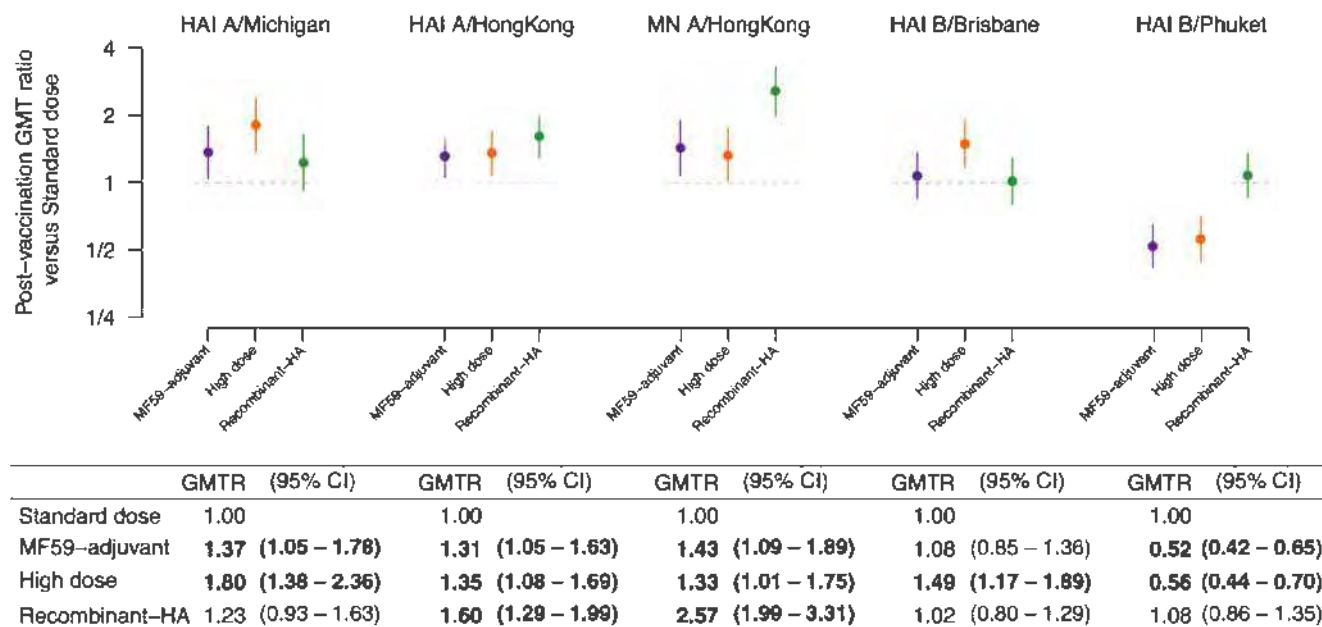
\*Values that are significantly different from the corresponding value in the standard-dose group. Statistical significance was designated at  $P$  value < .05.

Abbreviations: CI, confidence interval; D, day; GMT, geometric mean titer; HA, hemagglutinin; HAI, hemagglutination inhibition assay; MN, microneutralization assay; QIV, quadrivalent influenza vaccine; TIV, trivalent influenza vaccine.

<sup>a</sup>At least a 4-fold rise from D0 to D30 with D30 titer ≥40.

<sup>b</sup>Note that a B/Yamagata lineage virus was not included in the MF59-adjuvanted TIV and the high-dose TIV.





**Figure 2.** Comparisons of postvaccination geometric mean antibody titers in each of the enhanced vaccine groups, compared to the postvaccination geometric mean titer in the standard-dose QIV group ( $n = 200$  individuals per group). Values significantly different from 1.0 are highlighted in bold. Note that a B/Yamagata lineage virus was not included in the MF59-adjuvanted TIV and the high-dose TIV. Antigens used were A/Singapore/GP190B/2015 (A/Michigan/45/2015[H1N1]-like virus); A/Hong Kong/4801/2014(H3N2), with both egg-propagated and cell-propagated variants; B/Brisbane/60/2008, and B/Phuket/3073/2013. Abbreviations: CI, confidence interval; GMT, geometric mean titer; GMTR, geometric mean titer ratio comparing post-vaccination geometric mean titers between enhanced vaccine groups and the standard dose group; HA, hemagglutinin, HAI, hemagglutination inhibition assay; MN, microneutralization assay; QIV, quadrivalent influenza vaccine; TIV, trivalent influenza vaccine.

significant rises in T-cell responses from Day 0 to Day 30 were noted for the recombinant-HA vaccine against A(H1N1) and B/Victoria and for the MF59-adjuvanted vaccine against B/Victoria; no significant rises in the SD group were observed. IFN- $\gamma^+$  CD8 $^+$  T cells to B/Victoria increased from Day 7 to Day 30 for all 3 enhanced vaccines; this trend was statistically significant when contrasted with a decline in T cells among SD vaccinees.

For influenza-specific IFN- $\gamma^+$  CD4 $^+$  T-cell responses, statistically significant rises in T-cell responses were noted at 7 and/or 30 days postvaccination for the enhanced vaccines, though none of these were statistically significantly higher than the trend for the SD vaccine. Overall, the recombinant-HA vaccine caused sustained memory IFN- $\gamma^+$  CD4 $^+$  T-cell responses by significantly increased Day 30 mean fold rises for 3 of 3 viruses tested, whilst the HD vaccine increased CD4 $^+$  T-cell Day 30 memory fold rises for 2 of 3 viruses and the MF59-adjuvanted vaccine resulted in early Day 7 rises for 2 of 3 viruses and sustained memory rises for only 1 of 3 viruses. SD group had a significant rise in CD4 $^+$  T-cell response to 1 virus at day 7 and no significant rises for all 3 viruses tested at Day 30.

The rate of contraction of T-cell responses from acute Day 7 to memory Day 30 was determined by the fold change from Day 30, divided by Day 7 (Supplementary Appendix Table 5). We did not observe statistically significant contractions (or expansions) for virus-specific CD4 $^+$  T cells for any vaccines. For virus-specific CD8 $^+$  T cells, a significant difference for the fold

change from acute Day 7 to memory Day 30 responses was noted for B/Victoria only. Among those receiving the SD vaccine, B/Victoria-specific CD8 $^+$  T cells significantly contracted by 0.65-fold from 7 to 30 days postvaccination. In contrast, among those receiving the enhanced vaccines, B/Victoria-specific CD8 $^+$  T cells continued to increase by 1.34- to 1.40-fold from Day 7 to Day 30 ( $P$  values all  $< .05$ , compared to the standard vaccine group); therefore, enhanced vaccines maintained and expanded a larger pool of circulating B/Victoria-specific CD8 $^+$  T cells than the SD vaccine.

The most frequently reported adverse events following vaccination included local reactions, such as tenderness (range across vaccine groups, 12–20%), pain (10–22%) and swelling (4–10%; Supplementary Appendix Figure 4). Compared to the SD group, recipients of the MF59-adjuvanted vaccine and HD vaccine experienced more tenderness and recipients of the HD vaccine experienced more swelling, mostly of a mild nature. Hospitalizations were not uncommon, but the rates of postvaccination hospitalizations were not statistically different between the 4 vaccine groups (Supplementary Appendix Table 3). We did not identify any potentially vaccine-related serious adverse events.

## DISCUSSION

We found that all 3 of the 2017–2018 Northern hemisphere-enhanced vaccines had improved immunogenicity for influenza A(H1N1) and A(H3N2), compared to the SD vaccine, among

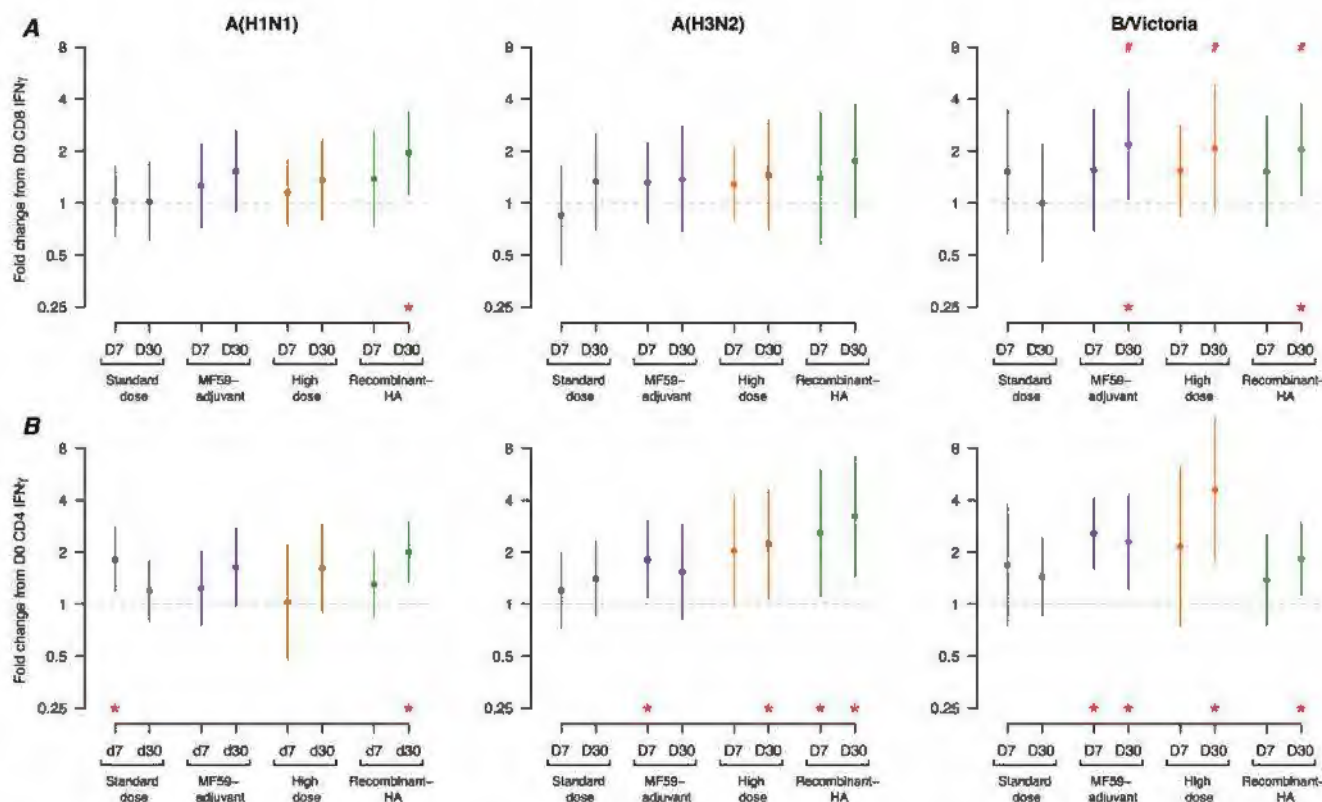
**Table 4. Proportions of Participants With Postvaccination Antibody Titers  $\geq 40$ ,  $\geq 80$ , and  $\geq 160$  in Each Group**

| Assay                            | Strain                          | Vaccination Group          |          |                              |          |                        |          |                             |          |
|----------------------------------|---------------------------------|----------------------------|----------|------------------------------|----------|------------------------|----------|-----------------------------|----------|
|                                  |                                 | Standard-dose QIV, n = 200 |          | MF59-adjuvanted TIV, n = 200 |          | High-dose TIV, n = 200 |          | Recombinant-HA QIV, n = 200 |          |
|                                  |                                 | Prop.                      | (95% CI) | Prop.                        | (95% CI) | Prop.                  | (95% CI) | Prop.                       | (95% CI) |
| Postvaccination (D30) titer ≥40  |                                 |                            |          |                              |          |                        |          |                             |          |
| HAI                              | A/Michigan/45/2015 (H1N1)       | 73%                        | (66–79%) | 82% *                        | (76–87%) | 83% *                  | (77–88%) | 76%                         | (69–81%) |
| HAI                              | A/Hong Kong/4801/2014 (H3N2)    | 94%                        | (90–97%) | 96%                          | (92–98%) | 96%                    | (92–98%) | 96%                         | (92–98%) |
| MN                               | A/Hong Kong/4801/2014 (H3N2)    | 78%                        | (72–84%) | 85%                          | (79–90%) | 82%                    | (77–87%) | 94% *                       | (90–97%) |
| HAI                              | B/Brisbane/60/2008              | 84%                        | (78–88%) | 88%                          | (83–93%) | 90%                    | (85–94%) | 88%                         | (82–92%) |
| HAI                              | B/Phuket/3073/2013 <sup>a</sup> | 94%                        | (90–97%) | 77% *                        | (71–83%) | 78% *                  | (72–84%) | 90%                         | (86–94%) |
| Postvaccination (D30) titer ≥80  |                                 |                            |          |                              |          |                        |          |                             |          |
| HAI                              | A/Michigan/45/2015 (H1N1)       | 54%                        | (47–61%) | 64% *                        | (57–71%) | 69% *                  | (62–75%) | 62%                         | (54–68%) |
| HAI                              | A/Hong Kong/4801/2014 (H3N2)    | 81%                        | (75–86%) | 88% *                        | (83–93%) | 88%                    | (82–92%) | 92% *                       | (89–96%) |
| MN                               | A/Hong Kong/4801/2014 (H3N2)    | 63%                        | (56–70%) | 72%                          | (65–78%) | 74% *                  | (67–79%) | 88% *                       | (83–92%) |
| HAI                              | B/Brisbane/60/2008              | 69%                        | (62–75%) | 70%                          | (63–76%) | 78%                    | (71–83%) | 64%                         | (57–71%) |
| HAI                              | B/Phuket/3073/2013 <sup>a</sup> | 76%                        | (69–81%) | 58% *                        | (51–65%) | 58% *                  | (51–65%) | 77%                         | (71–83%) |
| Postvaccination (D30) titer ≥160 |                                 |                            |          |                              |          |                        |          |                             |          |
| HAI                              | A/Michigan/45/2015 (H1N1)       | 35%                        | (28–42%) | 45% *                        | (38–52%) | 55% *                  | (48–62%) | 46% *                       | (39–53%) |
| HAI                              | A/Hong Kong/4801/2014 (H3N2)    | 64%                        | (56–70%) | 72%                          | (66–79%) | 75% *                  | (68–81%) | 81% *                       | (75–86%) |
| MN                               | A/Hong Kong/4801/2014 (H3N2)    | 48%                        | (41–56%) | 54%                          | (47–61%) | 58%                    | (51–65%) | 74% *                       | (68–80%) |
| HAI                              | B/Brisbane/60/2008              | 40%                        | (34–48%) | 44%                          | (37–52%) | 54% *                  | (46–61%) | 39%                         | (32–46%) |
| HAI                              | B/Phuket/3073/2013 <sup>a</sup> | 52%                        | (45–59%) | 32% *                        | (26–39%) | 33% *                  | (27–40%) | 56%                         | (49–63%) |

\*Significant differences in comparison to standard-dose QIV.

Abbreviations: D, day; HA, hemagglutinin; HAI, hemagglutination inhibition assay; MN, microneutralization assay; Prop., proportion; QIV, quadrivalent influenza vaccine; TIV, trivalent influenza vaccine.

<sup>a</sup>Note that a B/Yamagata lineage virus was not included in the MF59-adjuvanted TIV and the high-dose TIV.



**Figure 3.** The mean and standard deviations of the fold changes of Days 7 and 30 IFN- $\gamma$  T cells, compared to Day 0 responses for A/Michigan/45/2015(H1N1), A/Switzerland/9715293/2013(H3N2), and B/Brisbane/60/2008 viruses after *in vitro* stimulation for (A) CD8<sup>+</sup> and (B) CD4<sup>+</sup> IFN- $\gamma$  T cells ( $n = 20$  individuals per group). Values marked with a # symbol indicate a statistically significant difference ( $P < .05$ ), compared to the response in the standard-dose vaccine group at the same time point. Values marked with an \* indicate a statistically significant difference ( $P < .05$ ), compared to the baseline (Day 0) response within the same vaccine group. Abbreviations: D, day; HA, hemagglutinin; IFN, interferon.

older adults, while the recombinant-HA vaccine elicited a particularly high antibody response to the cell-like H3N2 strain, relative to the other enhanced vaccines and the SD vaccine (Figure 2). Improved CD4<sup>+</sup> T-cell responses against H3N2 were also seen at Day 7 or Day 30 for each enhanced vaccine (Figure 3). Influenza A(H3N2) virus infection causes the greatest morbidity and mortality effects in older adults [22] and there have been particular concerns in recent years over poorer vaccine effectiveness against influenza A(H3N2) [16, 23], which may be at least partially due to egg adaptations in A(H3N2) vaccine strains and/or poorer immunogenicity in repeated vaccinees [17, 24–27].

Enhanced vaccines resulted in higher antibody responses on almost all indicators, compared to a SD vaccine, to the A/Michigan/45/2015(H1N1)-like virus, which was introduced in the 2017–2018 season. The ratios of postvaccination titers against the A(H1N1) component for the MF59-adjuvanted vaccine and the HD vaccine, compared to the SD vaccine (1.37-fold higher and 1.80-fold higher, respectively), were very similar to pooled estimates in a recent meta-analysis for this ratio across previous immunogenicity trials (1.28 and 1.72, respectively) [5]. The antibody response to A(H1N1) among recombinant-HA

recipients in our study was better than the A(H1N1) response among older adults in a previous recombinant-HA trial [15]. Our findings for A(H3N2) were also within the range of postvaccination ratios for the HD vaccine and MF59-adjuvanted vaccine, compared to the SD vaccine, when observed across prior trials [5]. Our findings reinforce other studies suggesting that enhanced vaccines offer improved antibody responses over standard vaccines in older adults. However, our study was not designed to demonstrate efficacy against polymerase chain reaction–confirmed influenza, and comparisons of clinical efficacy and effectiveness are still needed.

However, the findings for influenza B viruses were less clear. Antibody responses to the influenza B/Victoria-lineage component, which was in the TIV and QIV formulations in 2017–2018 and the previous season, were high for all vaccines. There were also significant improvements over the SD vaccine in CD8<sup>+</sup> T-cell responses to B/Victoria (Figure 3). Not surprisingly, the quadrivalent SD vaccine resulted in higher antibody responses to the influenza B/Yamagata-lineage strain, compared to the trivalent MF59-adjuvanted and HD vaccines, which did not include this component; nonetheless, both vaccines were associated with significant rises in B/Yamagata titers (Table 3). The



QIV recombinant-HA vaccine did not result in a higher antibody response to the influenza B/Yamagata lineage, compared to the QIV SD vaccine, consistent with a previous trial [13].

Our study had a number of limitations. First, vaccine immunogenicity is not equivalent to vaccine efficacy or effectiveness, nor is there yet a way to directly extrapolate our findings into an epidemiologic measure of differences in actual vaccine protection. Second, we only tested sera from a subset of 800 participants, determining that this would be sufficient to compare vaccines in the first year and allowing us to save more of the sera for future cross-season analyses. Two-thirds of participants were vaccinated during the previous season; examining the association between vaccination histories and immune response will also require additional future testing. Finally, here we only examined the immediate response to vaccination; we did not examine the duration of protection or effects on subsequent vaccinations with enhanced or SD vaccines.

In conclusion, this randomized, controlled trial provides a unique comparison of the immune response to multiple enhanced influenza vaccine options for older adults. Although distinguishing the relative preventive value of alternative vaccine types among older adults will ultimately depend on future efficacy trials and/or well-controlled effectiveness studies, the findings from this ongoing immunogenicity trial can help to establish the conditions for those more definitive evaluations, including what differences in efficacy/effectiveness might plausibly be expected.

### Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

### Notes

**Author contributions.** B. J. C. and M. G. T. designed the study and drafted the paper. B. J. C. wrote the statistical analysis plan and is the guarantor. R. A. P. M. P., S. A. V., and A. P. Y. L. conducted laboratory testing. B. J. C., M. G. T., N. H. L. L., and A. D. I. designed the data collection tools. Y. H. T. and J. H. E. W. implemented the trial. V. J. F. cleaned and analyzed the data. B. J. C., M. G. T., N. H. L. L., A. D. I., H. C. S. and D. K. M. I. monitored the data collection for the whole trial. B. J. C., R. A. P. M. P., S. A. V., N. H. L. L., A. D. I., A. P. Y. L., E. A.-B., A. M. F., M. Z. L., S. G., S. S., I. G. B., D. M. S., J. S. M. P., and M. G. T. interpreted the data. All authors revised the paper.

**Acknowledgments.** The authors thank Ed Belongia for advice on the study design and implementation; the study staff for assistance in project implementation, including Tin-Kin Chau, Faith Ho, Jennifer Ho, Fiona Kee, Janisy Lai, Cecily Leung, Anita Li, Jessamine Luk, Lorella Mak, Yvonne Ng, Angel Wong, Miyuki Wong, Phoebe Wong, and Kitty Yu; Leo Luk, Emily Yau, Chi Tsang, and Kin Chan for laboratory support; Julie Au and Chi-Kin Lam for administrative support; and David Shay and Jerome Tokars for feedback on an earlier version of this manuscript.

**Disclaimer.** The sponsor had no role in the data collection and analysis, or the decision to publish, but was involved in the study design and preparation of the manuscript. The contents of this report are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

**Financial support.** This study was supported by the Centers for Disease Control and Prevention (Cooperative Agreement Number IP001064-02).

**Potential conflicts of interest.** B. J. C. has received honoraria from Sanofi and Roche for advisory committees. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

### References

- Barberis J, Martini M, Iavarone F, Orsi A. Available influenza vaccines: immunization strategies, history and new tools for fighting the disease. *J Prev Med Hyg* 2016; 57:E41–6.
- Talbot HK, Niao H, Zhu Y, Chen Q, Williams IV, Griffin MR. Clinical effectiveness of split-virion versus subunit trivalent influenza vaccines in older adults. *Clin Infect Dis* 2015; 60:1170–5.
- Belongia EA, Simpson MD, King JP, et al. Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test-negative design studies. *Lancet Infect Dis* 2016; 16:942–51.
- Xu C, Thompson MG, Cowling BJ. Influenza vaccination in tropical and subtropical areas. *Lancet Respir Med* 2017; 5:920–2.
- Ng TWY, Cowling BJ, Gao HZ, Thompson MG. Comparative immunogenicity of enhanced seasonal influenza vaccines in older adults: a systematic review and meta-analysis. *J Infect Dis* 2019; 219:1525–35.
- Wong SS, Webby RJ. Traditional and new influenza vaccines. *Clin Microbiol Rev* 2013; 26:476–92.
- Schaffner W, van Buynnder P, McNeil S, Osterhaus ADME. Seasonal influenza immunisation: Strategies for older adults. *Int J Clin Pract* 2018; 72:e13249.
- Gasparini R, Pozzi T, Montomali E, et al. Increased immunogenicity of the MF59-adjuvanted influenza vaccine compared to a conventional subunit vaccine in elderly subjects. *Eur J Epidemiol* 2001; 17:135–40.
- Camilloni B, Basileo M, Valente S, Nunzi E, Iorio AM. Immunogenicity of intramuscular MF59-adjuvanted and intradermal administered influenza enhanced vaccines in subjects aged over 60: a literature review. *Hum Vaccin Immunother* 2015; 11:553–63.
- Khurana S, Verma N, Yewdell JW, et al. MF59 adjuvant enhances diversity and affinity of antibody-mediated immune response to pandemic influenza vaccines. *Sci Transl Med* 2011; 3:85ra48.
- Couch RB, Winokur P, Brady R, et al. Safety and immunogenicity of a high dosage trivalent influenza vaccine among elderly subjects. *Vaccine* 2007; 25:7656–63.
- DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. *N Engl J Med* 2014; 371:635–45.
- Keitel WA, Treanor JJ, El Sahly HM, et al. Comparative immunogenicity of recombinant influenza hemagglutinin (rHA) and trivalent inactivated vaccine (TIV) among persons > or =65 years old. *Vaccine* 2009; 28:379–85.
- Treanor JJ, Schiff GM, Couch RB, et al. Dose-related safety and immunogenicity of a trivalent baculovirus expressed influenza virus hemagglutinin vaccine in elderly adults. *J Infect Dis* 2006; 193:1223–8.
- Dunkle LM, Izikson R, Patriarca P, et al. Protein Sciences Consortium 12 Study Team. Efficacy of recombinant influenza vaccine in adults 50 years of age or older. *N Engl J Med* 2017; 376:2427–36.
- Rondy M, El Oneiri N, Thompson MG, Levêque A, Moren A, Sullivan SG. Effectiveness of influenza vaccines in preventing severe influenza illness among adults: a systematic review and meta-analysis of test-negative design case-control studies. *J Infect* 2017; 75:381–94.
- Skowronski DM, Janjua NZ, De Serres G, et al. Low 2012–13 influenza vaccine effectiveness associated with mutation in the egg-adapted H3N2 vaccine strain not antigenic drift in circulating viruses. *PLOS One* 2014; 9:e92153.
- McElhaney JE, Xie D, Hager WD, et al. T cell responses are better correlates of vaccine protection in the elderly. *J Immunol* 2006; 176:6333–9.
- Kuntar A, McElhaney JE, Walrond L, et al. Cellular immune responses of older adults to four influenza vaccines: results of a randomized, controlled comparison. *Hum Vaccin Immunother* 2017; 13:2048–57.
- Tam YH, Valkenburg SA, Perera RAPM, et al. Immune responses to twice-annual influenza vaccination in older adults in Hong Kong. *Clin Infect Dis* 2018; 66:904–12.
- Cumming G. Inference by eye: reading the overlap of independent confidence intervals. *Stat Med* 2009; 28:205–20.
- Wu P, Presanis AM, Rond HS, Lau EHY, Fang VJ, Cowling BJ. A joint analysis of influenza-associated hospitalizations and mortality in Hong Kong, 1998–2013. *Sci Rep* 2017; 7:929.
- Russell K, Chung JR, Monto AS, et al. Influenza vaccine effectiveness in older adults compared with younger adults over five seasons. *Vaccine* 2018; 36:1272–8.

24. Skowronski DM, Chambers C, Sabaiduc S, et al. A perfect storm: impact of genomic variation and serial vaccination on low influenza vaccine effectiveness during the 2014–2015 season. *Clin Infect Dis* **2016**; 63:21–32.
25. Skowronski DM, Chambers C, De Serres G, et al. Early season co-circulation of influenza A(H3N2) and B(Yamagata): interim estimates of 2017/18 vaccine effectiveness, Canada, January 2018. *Euro Surveill* **2018**; 23.
26. Cobey S, Gouma S, Parkhouse K, et al. Poor immunogenicity, not vaccine strain egg adaptation, may explain the low H3N2 influenza vaccine effectiveness in 2012–2013. *Clin Infect Dis* **2018**; 67:327–33.
27. Zost SJ, Parkhouse K, Gumina ME, et al. Contemporary H3N2 influenza viruses have a glycosylation site that alters binding of antibodies elicited by egg-adapted vaccine strains. *Proc Natl Acad Sci USA* **2017**; 114:12578–83.

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Sent:** Thu, 30 Apr 2020 14:35:27 +0000  
**To:** (b)(6)  
**Subject:** checking in

Do we need to check in before today's call?

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Sent:** Sun, 10 May 2020 17:14:07 +0000  
**To:** Santos, Michael (FNIH) [T]; Jansen, Kathrin  
**Cc:** Schrag, Stephanie (CDC/DDID/NCIRD/DBD); Verani, Jennifer R. (CDC/DDID/NCIRD/DBD); Thornburg, Natalie (CDC/DDID/NCIRD/DVD); Erbeling, Emily (NIH/NIAID) [E]  
**Subject:** RE: Review requested: Human Challenge Model draft; notes from Vaccines Sub-Groups, ACTIV Leadership Team, and Preclinical WG

Michael and Kathrin

To ensure that CDC can provide the level of input which is being requested, please add Stephanie Schrag and Jennifer Verani, who are leading CDC coronavirus vaccine evaluation activities, and Natalie Thornburg, who leads COVID serology activities, to the overall ACTIV group. I think that Stephanie and Jennifer would be helpful additions to the subgroup considering the design of a phase III study. Kathrin has been asking for information about ongoing natural history and serology studies and Natalie would be well placed to discuss CDC's work.

I can send them some of the notes from the previous meetings so they can get caught up but I was wondering if you have that posted somewhere that they could access, if that's easier.

Thank you,  
Nancy

---

**From:** Santos, Michael (FNIH) [T] <msantos@fnih.org>  
**Sent:** Saturday, May 9, 2020 10:16 PM  
**To:** (b)(6) Lowy, Douglas (NIH/NCI) [E] <LowyD@mail.nih.gov>;  
(b)(6) Arvin, Ann <aarvin@stanford.edu>; Beth Bell (b)(6)  
(b)(6) susan.buchbinder@sfdph.org; lcorey@fredhutch.org; mmdavis@stanford.edu;  
Emilio.Emini@gatesfoundation.org; (b)(6) Haynes, Barton  
<hayne002@mc.duke.edu>; hotez@bcm.edu; lanzavecchia@irb.usi.ch; Marks, Peter (FDA/CBER)  
<Peter.Marks@fda.hhs.gov>; Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Messonnier, Nancy  
(CDC/DDID/NCIRD/OD) <nar5@cdc.gov>; Michael, Nelson L CIV USARMY MEDCOM WRAIR (USA)  
<nelson.l.michael2.civ@mail.mil>; Offit, Paul <offit@email.chop.edu>; HSchuite@its.jnj.com; Seals,  
Jonathan (OS/ASPR/BARDA) <jonathan.seals@hhs.gov>; (b)(6) Tal Zaks  
(b)(6)  
**Cc:** Tolman, Brett <btolman@deloitte.com>; Austin, Sarah (NIH/NIAID) [E] <austinsj@niaid.nih.gov>;  
(b)(6) Shannon.Devine@duke.edu; (b)(6) Johnson, Maureen  
(NIH/NCI) [E] <johnsonr@dea.nci.nih.gov>; Kozlowski, Mary (NIH/NCI) [C] <mary.kozlowski@nih.gov>;  
bminnich@fredhutch.org; (b)(6) kelly.soderberg@duke.edu;  
Douglas.SorianoOsejo@bcm.edu; Suhana, Tina (NIH/VRC) [E] <esuhana@mail.nih.gov>;  
(b)(6) Cohen, Myron <myron\_cohen@med.unc.edu>;  
Douoguih, Macaya [JRDUS] <MDouogui@its.jnj.com>; Erbeling, Emily (NIH/NIAID) [E]  
<emily.erbeling@nih.gov>; Gilbert PhD, Peter B <pgilbert@scharp.org>; Paul Gillard  
(b)(6) Gruber, Marion (FDA/CBER)  
<Marion.Gruber@fda.hhs.gov>; Gurunathan, Sanjay /US <(b)(6)>; Hamilton,



Holli (OS/ASPR/BARDA) <Holli.Hamilton@hhs.gov>; (b)(6); Ledgerwood, Julie (NIH/NIAID) [E] <JUMARTIN@niaid.nih.gov>; Leyssen, Maarten [JRDNL] <MLEyssen@its.jnj.com>; Marovich, Mary (NIH/NIAID) [E] <mary.marovich@nih.gov>; Kathleen Neuzil <kneuzil@som.umaryland.edu>; Robb, Merlin <mrobb@hivresearch.org>; Sahin@Uni-Mainz.de; Michael Watson (x) <(b)(6)>; Parker, Ashley (NIH/OD) [E] <ashley.parker@nih.gov>; Qashu, Felicia (NIH/OD) [E] <felicia.qashu@nih.gov>; Colvis, Christine (NIH/NCATS) [E] <Christine.Colvis@nih.gov>; (b)(6); (b)(6) Kurilla, Michael (NIH/NCATS) [E] <michael.kurilla@nih.gov>; Read, Sarah (NIH/NIAID) [E] <readsa@niaid.nih.gov>; (b)(6) Menetski, Joseph (FNIH) [T] <jmenetski@fnihi.org>; Alvarez, Rosa Maria (b)(6); Adam, Stacey (FNIH) [T] <sadam@fnihi.org>; Kim, Elizabeth (b)(6) Tountas, Karen (FNIH) [T] <ktountas@fnihi.org>; Wachtel, Jonathan (b)(6) Wholley, David (FNIH) [T] <dwholley@fnihi.org>; Gonzalez, Nina (b)(6); Stratton, Benjamin (b)(6)

**Subject:** Review requested: Human Challenge Model draft; notes from Vaccines Sub-Groups, ACTIV Leadership Team, and Preclinical WG

Dear Vaccines Working Group members (and cc'ing others for awareness),

This note is an omnibus update for the Working Group: Sub-Group meeting notes, the human challenge model draft and agenda for the Working Group meeting, upcoming Vaccines Clinical Trial Sub-Group meetings and topics, and for awareness notes from the ACTIV Leadership Team meeting and Preclinical WG.

#### Sub-Group meeting notes

As a reminder, the Protective Immune Responses and Vaccine-associated Immune Enhancement Sub-Groups met since our last Working Group meeting (Thurs and Fri, respectively). Thank you to all who participated or sent input. **Attached are the notes and action items from each meeting.** The agendas and meeting materials and pre-reads are embedded in those documents. If anyone would like to be added to the lists for either Sub-Group, please let us know.

#### **Review Controlled Human Infection Model outline** in preparation for Monday's Working Group meeting

The main agenda item at the next Vaccines Working Group meeting, Monday, 12pm ET (9am PT / 6pm CEST), is a discussion of the Working Group's perspective on a CoV-2 controlled human infection model. Please review the attached outline to prepare for that discussion. If you cannot attend the meeting, feel free to send input via email that we can represent.

#### Vaccines Clinical Trial Sub-Group updates

Members of this Sub-Group are invited on Tuesday (11am ET) to join the Clinical Trial Capacity Working Group meeting, where Paula and Larry will share the plans of the Sub-Group and the CTC WG will share their activities and how they can work with us (e.g., inventory trial site capacity). **The Sub-Group meeting Wednesday (1pm ET) will focus on key protocol questions.**

#### ACTIV Leadership Team meeting notes

Last Wednesday, the ACTIV Leadership Team (the parent body above the Working Groups) met. Kathrin and Doug presented the progress and plans of the Working Group and answered questions. The meeting presentation and notes are attached. **Note: This is a good way to see a high-level summary of**



the activities of the other Working Groups, many of which are relevant to our work; if you have specific questions, let us know and we can follow up.

Pre-clinical Working Group

Finally, as discussed last week we will continue to share notes from the Preclinical Working Group for awareness (attached zip file). **Note: a request to review the data collection fields for animal models will be coming to our group**, which we will circulate to the Protective Immune Responses and Vaccine-associated Immune Enhancement Sub-Groups.

As always, please don't hesitate to reach out with any questions or suggestions.

Best regards,  
Brett and Mike

**Michael Santos, PhD**

Associate Vice President, Science

**Foundation for the National Institutes of Health**

301-402-6917 | [fnihi.org](http://fnihi.org)

11400 Rockville Pike, Suite 600, North Bethesda, MD 20852



Stay at the forefront of FNIH news: [fnihi.org/newsletter](http://fnihi.org/newsletter)

**From:** Grabenstein, John D.  
**Sent:** Wed, 21 Dec 2016 16:57:01 -0500  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** RE: amazing

Well, not what I had in mind in terms of a holiday present.

Thanks for considering our position. I'm sure you'll act wisely and prudently.

Best wishes for the holidays and new year!

John

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [mailto:nar5@cdc.gov]  
**Sent:** Wednesday, December 21, 2016 16:55  
**To:** Grabenstein, John D.  
**Subject:** amazing

John,

When I saw you in October, you told me I would be receiving a letter from MERCK. I just got it yesterday, dated September, with a postmark from September. I can find no information about when it arrived at CDC or where it has been in the past 4 months. But I now have it and will respond.

Happy holidays to you.

Nancy

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Phil Watson  
**Sent:** Fri, 3 Feb 2017 20:11:31 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD); Patricia Novy  
**Cc:** Hadler, Stephen (CDC/OID/NCIRD); Mahon, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: Follow-up: GSK Advisory Board

Dear Dr Messonnier,

Thanks very much for your introductory email, and for confirming that CDC is willing to provide information. This is very much appreciated and will be extremely helpful both for GSK colleagues and for external experts attending the advisory board meeting.

Dr Hadley and Dr Mahon,

In the first instance, may I suggest that we arrange a teleconference one day next week (Tues Feb 6 – Fri Feb 10) – so that I can provide some background information and we can align on expectations? I'll be travelling in Europe on business, but happy to be flexible on timing to accommodate your availability. Please let me know when might be convenient and I can provide TC details.

I look forward to speaking with you soon.

Kind regards,  
Phil

**Phil Watson**  
**Director, Global Medical Affairs - Neisseria**

GlaxoSmithKline Vaccines  
14200 Shady Grove Road | Rockville, MD 20850 | U.S.A.

**Office:** (b)(6) | **Cell:** (b)(6) | **Email:** (b)(6)

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [mailto:nar5@cdc.gov]  
**Sent:** Thursday, February 02, 2017 5:23 PM  
**To:** Patricia Novy  
**Cc:** Phil Watson; Hadler, Stephen (CDC/OID/NCIRD); Mahon, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: Follow-up: GSK Advisory Board

**EXTERNAL**

Patricia,

Thank you for the follow up. As we discussed, CDC is happy to provide information about US epidemiology and laboratory analysis. By way of email, let me introduce you to Steve Hadler, who is acting Branch Chief of the Meningitis Branch, who can be your POC. Let me also introduce you to Barbara Mahon, who is the new Director for Division of Bacterial Diseases at CDC. We don't have subject matter responsibility for GC but can connect with those folks as well.

Nancy

**From:** Patricia Novy [mailto:(b)(6)]  
**Sent:** Tuesday, January 31, 2017 7:05 PM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>  
**Cc:** Phil Watson (b)(6)  
**Subject:** Follow-up: GSK Advisory Board

Dear Messonnier,

In previous discussions, I highlighted GSK's intention to hold an advisory board meeting, and we discussed the feasibility of CDC representatives attending to present relevant epidemiological data.

It is now confirmed that the meeting will take place in Atlanta on April 6<sup>th</sup> and 7<sup>th</sup>, and the agreed meeting objectives are:

- To review emerging data relating to MenB vaccines and seek input to design further studies/ analyses that will bridge current gaps in understanding.
- To review available phase II data for Men ABCWY vaccine and discuss schedule options to guide future development.

- To discuss findings relating to gonorrhoea, and seek input to design studies in US allowing further investigation of MenB-4C's impact on gonorrhea.

In this context, it would also very valuable to provide the attendees with the most recent data relating to US disease epidemiology, strain analysis and antimicrobial resistance – both for meningococcal and gonococcal disease.

I'm therefore writing to ask whether it might be possible for anyone from CDC to deliver presentations on each of these topics during the course of the meeting?

If so, I'd be very grateful if you could advise on the appropriate individuals to invite, and/ or provide guidance on the appropriate next steps. Also copied on this email is Phil Watson, the US Medical Affairs Lead for Neisseria.

Thanks for giving this your consideration,

Patricia Novy, PhD

Medical Affairs Scientific Director -- Vaccines

US Medical Affairs

GSK

Email

Mobile

(b)(6)

**GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.**

**GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.**



**From:** Leonard Friedland  
**Sent:** Wed, 15 Feb 2017 19:56:16 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD); Cohn, Amanda (CDC/OID/NCIRD)  
**Subject:** Contact with influenza WG

Dear Nancy and Amanda,

Amanda, I had the opportunity to speak with Nancy last week at NVAC where I mentioned that my GSK influenza colleagues have contacted Lisa Grohskopf and Joe Bresee to notify the flu ACIP WG of new clinical trial data (clinical endpoint study of Fluarix Quad in 6-35 mos olds) and to inquire if the WG would be interested in a presentation on these data. We also contacted Lisa and Joe to bring to their attention a question we are hearing from providers about ACIP recommendations for FluLaval in young infants (copied at the bottom). We have not received acknowledgment of the messages.

Nancy asked that I forward the messages to you both.

Thank you for mentioning to Lisa and Joe GSK's interest to present and discuss these clinical endpoint data with the flu WG.

Best regards, Len

---

**From:** Catia Ferreira  
**Sent:** Wednesday, January 25, 2017 1:27 PM  
**To:** 'Grohskopf, Lisa A. (CDC/OID/NCIRD)' ([llkg6@cdc.gov](mailto:llkg6@cdc.gov))' <[llkg6@cdc.gov](mailto:llkg6@cdc.gov)>; 'Bresee, Joseph (CDC/OID/NCIRD)' <[jsb6@cdc.gov](mailto:jsb6@cdc.gov)>  
**Cc:** Luis Romano (b)(6)  
**Subject:** Confidential: New EFFICACY data from large randomized clinical trial for prevention of influenza in children 6-35 months  
**Importance:** High

Dear Lisa and Joe,

We are very pleased to announce that we have new data available for presentation to the influenza working group, detailing the efficacy of Influenza prevention in the youngest risk group.

"A phase III, observer-blind, randomized, multi-country, non-influenza vaccine comparator-controlled study to demonstrate the efficacy of GSK Biologicals' quadrivalent seasonal influenza candidate vaccine GSK2321138A (FLU D-QIV), administered intramuscularly in children 6 to 35 months of age"

(b)(4)

(b)(4)

We would like to ask if at all possible a time for presentation to the working group whenever the opportunity is available. If you could let us know when this would be a good time we will initiate materials for this meeting for pre-read and presentation. As you can imagine this is a fairly extensive and complex clinical trial and it may require a few sessions in order to appropriately digest the data, but we can discuss how best to section of the pieces relevant to the group.

Additionally, please see bellow, we are still hearing feedback of some confusion and feel is important to continue to highlight this information,

With our very best regards,

Catia Ferreira on behalf of the GSK Influenza team

---

**From:** Luis Romano

**Sent:** Thursday, January 12, 2017 5:32 PM

**To:** Grohskopf, Lisa A. (CDC/OID/NCIRD) <[lk66@cdc.gov](mailto:lk66@cdc.gov)>; Bresee, Joseph (CDC/OID/NCIRD) <[jsb6@cdc.gov](mailto:jsb6@cdc.gov)>

Cc: Catia Ferreira (b)(6)  
Subject: FluLaval QIV publication and question about AIC "Ask the Experts"

Dear Lisa and Joe

Happy New Year!

We would like to share with you that the FluLaval Q-QIV-022 study manuscript has been published (advance access) in the Journal of the Pediatric Infectious Diseases Society (JPIDS).

As you know, this study generated the pivotal data that supported the FluLaval Quadrivalent extended age indication for its use in children 6-35 mo.

DOI: 10.1093/jpids/piw068  
<http://jpids.oxfordjournals.org/content/early/2017/01/05/jpids.piw068.abstract?sid=532a9352-6856-48b9-bf3e-431024a542df>

Title: Time to change dosing of inactivated quadrivalent influenza vaccine in young children: evidence from a phase III, randomized, controlled trial

Authorship: Jain VK, Domachowske J, Wang L, Ofori-Anyinam O, Rodriguez Weber MA, Leonardi M, Klein N, Schlichter G, Jeanfreau R, Haney B, Chu L, Harris J-A, Sarpong K, Micucio AC, Soni J, Chandrashekar V, Li P, Innis BL

We would also appreciate your feedback regarding some questions and comments we have received around the last paragraph included in one of the answers from the recent AIC's "Ask the Experts" section on FluLaval Quadrivalent (see below)

### ***Influenza Vaccine***

---

***Q: Please provide details about the use of FluLaval influenza vaccine (GlaxoSmithKline) in children younger than 3 years.***

***A:*** On November 18, 2016, the Food and Drug Administration approved an extension of the age range of quadrivalent FluLaval (inactivated influenza vaccine, GSK) to include children 6 through 35 months of age. FluLaval was previously approved for people 3 years of age and older. The approval of the extended age range for FluLaval was based on a study showing an equivalent ("non-inferior") response compared to children who received Fluzone (Sanofi Pasteur) pediatric formulation. The vaccine will be supplied for this indication in manufacturer-filled syringes and multi-dose vials. The dosage approved for children 6 through 35 months of age is 0.5 mL—the same dosage as for people 3 years of age and older.

ACIP has not yet issued a recommendation regarding the use of FluLaval in children 6 through 35 months of age. However, clinicians are free to use this and other vaccines in a manner consistent with their labeling



Apparently, the phrase “ACIP has not yet issued a recommendation regarding the use of FluLaval in children 6 through 35 months of age” is creating some confusion, as it might be interpreted that the use of FluLaval QIV in this age group is not supported by ACIP. As CDC now includes FluLaval QIV’s 6mo-3 yr schedule in its official influenza vaccines table , we do consider it to be part of the influenza vaccines recommended by CDC.

Since IAC informed us that the information included in their “Ask the Experts” section is first reviewed by CDC, we wanted to share these concerns with you and kindly ask for your feedback before contacting IAC.

Thank you!

With our best regards,

Luis Romano and Catia Ferreira on behalf of the GSK Influenza team.

**Luis Romano, MD**  
**Medical Affairs Director, Vaccines**  
Influenza Vaccine Medical  
Research & Development

**GSK**  
5 Crescent Drive, Philadelphia, PA 19112, United States

**Email** (b)(6)  
**Mobile**

[gsk.com](http://gsk.com) | [Twitter](https://twitter.com/gsk) | [YouTube](https://www.youtube.com/gsk) | [Facebook](https://www.facebook.com/gsk) | [Flickr](https://www.flickr.com/photos/gsk/)



**GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.**

**From:** Grabenstein, John D.  
**Sent:** Thu, 23 Feb 2017 14:06:34 -0500  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** Re: ?

Happy to do so in any capacity.

My new work phone is (b)(6)

Cell (b)(6)

At Atlanta airport for the next hour.

John

From mobile phone ...

John D. Grabenstein, RPh, PhD

Executive Director, Global Health & Medical Affairs

Merck Vaccines

(b)(6)

On Feb 23, 2017, at 13:57, Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)> wrote:

John,

I was talking to the new chair of NVAC who was interested in some questions about DOD and vaccine stockpiles. It seemed like it would be helpful for her to talk to someone with historic knowledge of DOD and vaccines to know if this has been previously considered but also about who makes such decisions at DOD. I, of course, immediately thought of you. I wondered if you would be willing to talk to her on background? Unofficially of course.

Nancy

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Grabenstein, John D.  
**Sent:** Thu, 23 Feb 2017 13:57:53 -0500  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** Out of Office: ?

I am out of the main office from Feb 22 through Feb 23. I'll be checking email when no one is looking.  
I will be back at my desk on Friday morning, February 24, 2017.

If you need immediate assistance, please contact faithful and resourceful Linda Tierney at (b)(6)  
Or consult my talented associates, Barb Kuter (Ped-Adol), Gonzalo Perez (RDMAs), Eddy Bresnitz (Adult), or  
Kathleen Taylor (USVMA), at (b)(6)

Keep in touch and keep vaccinating!  
John

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Grabenstein, John D.  
**Sent:** Tue, 23 May 2017 10:13:32 -0400  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** telephone

Cell [REDACTED]  
Desk [REDACTED]

Thx, John

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Vaccines, UG-2B09  
351 N. Sumneytown Pike  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk [REDACTED]

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** (b)(6)  
**Sent:** Thu, 1 Jun 2017 12:23:07 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: Flu and beyond

Great. Thank you, Nancy.

Barbara –

I'm sure scheduling won't be easy. To be able to speak sooner than later, please let me know 1 or 2 times that might work and I'll rearrange my schedule.

Julian

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [mailto:nar5@cdc.gov]  
**Sent:** Wednesday, May 31, 2017 3:47 PM  
**To:** Ritchey, Julian /US  
**Cc:** Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: Flu and beyond

Sure. It would be great to talk. I'm cc'ing my admin assistant to help with scheduling.  
Nancy

---

**From:** (b)(6)  
**Sent:** Tuesday, May 30, 2017 9:03 AM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Subject:** Flu and beyond

Dear Nancy –

I hope this finds you well after a restful Memorial Day weekend.

Would it be possible to connect with you via a phone call at your convenience (a relative term, I know!) to share with you discussions we are having around Fluzone HD and some aspects of this that some of us think might be "a-ha" opportunities going forward? Building off your comments at the Flu Summit I thought a phone call could be beneficial on a multiple levels.

Please let me what would work for you and I'm happy to adjust accordingly.

Regards,  
Julian

**From:** Grabenstein, John D.  
**Sent:** Tue, 2 May 2017 17:03:31 -0400  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Kuter, Barbara J.; Yoder, Gregory A  
**Subject:** Presentation on Merck candidate vaccine pipeline

CAPT Messonnier,

In the next few days, I would like to give you a call to discuss broad parameters for how to offer CDC a presentation on the status of Merck's investigational vaccine pipeline.

One of my colleagues has already asked our lawyers and one of your lawyers to refresh a confidentiality agreement.

- who should attend, how many
- when, narrowing down date ranges that would work for you
- where, in a CDC meeting room perhaps, without any off-site projection

If you might like to suggest a few times, I will rearrange my calendar accordingly.

Best regards, John

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Vaccines, UG-2B09  
351 N. Sumneytown Pike  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk + (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.



**From:** Grabenstein, John D.  
**Sent:** Mon, 26 Jun 2017 17:08:57 -0400  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Limbago, Brandi (CDC/OID/NCIRD); Cohn, Amanda (CDC/OID/NCIRD)  
**Subject:** RE: Thank you from the Merck Team

CAPT Messonnier, could you please forward to CDR Patel?

Projected questions regarding CMV infection (CMVi) and congenital CMV (cCMVi) ...

- Is the CDC doing any work to better understand the link between CMVi and cCMVi? Any surveillance work? Any planned studies?
- What parameters would CDC anticipate being relevant as it considers vaccination options, given trial endpoint of CMV infection in young women (as obligate precursor to congenital CMV infection and disease)?
  - What additional evidence (real-world, epidemiological, clinical) could be relevant?
- Do you have concerns with regards to target population (girls and young women 9 through 35 years of age)?
  - What are your thoughts regarding feasibility of vaccine implementation using the adolescent vaccination platform?
- If a point-of-care test is required to identify need for vaccination among young women, would this be a major barrier to implementation and vaccine uptake?
- Population health models (T. Lanzieri et al., *Vaccine* 2014) suggest vaccination of toddlers may have the greatest impact on cCMV prevention. How could this be addressed in the absence of direct evidence of infection prevention in this cohort?

---

**From:** Grabenstein, John D.  
**Sent:** Saturday, June 24, 2017 17:59  
**To:** Cohn Amanda (CDC/OID/NCIRD); Limbago Brandi; 'Nancy Rosenstein MD (NAR5@CDC.GOV)'; (melinda.wharton@cdc.hhs.gov); 'afc0@cdc.gov'; 'shp5@cdc.gov'  
**Cc:** Draghia, Ruxandra; Annunziato, Paula W.; Kuter, Barbara J.; Collier, Beth-Ann Griswold; Kaplan, Susan; Yoder, Gregory A; Musey, Luwy; Bresnitz, Eddy A.; Roberts, Craig; Saddier, Patricia  
**Subject:** Thank you from the Merck Team

CAPT Messonnier, CDR Cohn, and all,

On behalf of the Merck vaccine pipeline team, I wanted to thank you for your time and discussion during our visit on Tuesday, June 20. Our team appreciated the opportunity to update you and hear your scientific perspectives.

The heart of what we do is to develop vaccines that fundamentally improve the public's health. Your counsel helps us.

We heard several voices suggest that repeat discussions, in roughly a year, could be advantageous to your team and to ours.

Next week, we'll follow-up on the various notes and to-dos we jotted down.

With professional thanks,

John

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Vaccines, UG-2B09  
351 N. Sumneytown Pike  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.



**From:** Ogden, Lydia  
**Sent:** Fri, 28 Jul 2017 13:49:38 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Pope, Kristin (CDC/OID/NCIRD)  
**Subject:** Request to schedule a call

Nancy: Mike Nally, President of Merck Vaccines, and I would like to schedule a call with you on HPV vaccine supply as soon as your schedule permits. I'd think 30 minutes would be more than sufficient. Can you please let me know who manages your calendar? Thanks so much. Lydia

Lydia L. Ogden, PhD, MPP  
Senior Executive Director  
Global Vaccine Policy, Partnerships & Government Relations  
Merck  
Voice and text: (b)(6)  
Email: (b)(6)  
Assistant: Betsy Opdyke  
(b)(6)  
Voice: (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Carroll, Judy on behalf of "Draghia, Ruxandra" (b)(6)  
**Sent:** Mon, 11 Sep 2017 19:25:53 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD); Cohn, Amanda (CDC/OID/NCIRD)  
**Cc:** Dooling, Kathleen L.  
(CDC/OID/NCIRD); nancy\_bennett@urmc.rochester.edu; Bresnitz, Eddy A.  
**Subject:** Herpes Zoster Vaccines Discussion, ACIP Meeting, June 21, 2017, Revaccination Policy  
**Attachments:** CDC HZ 091117 letter.pdf

Dear Drs. Messonnier and Cohn,

Please see the attached letter for your consideration.

Thank you,

Ruxandra Draghia, MD, PhD  
Vice President  
Public Health & Scientific Affairs  
Global Vaccines

P: (b)(6)  
M: (b)(6)

Assistant: Judy Carroll (b)(6)  
(b)(6)  
[merck.com](http://merck.com)



**MERCK**

INVENTING FOR LIFE



Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error,

please notify us immediately by reply e-mail and then delete it from your system.

(b)(4)

(b)(4)

(b)(4)



(b)(4)

**From:** (b)(6)  
**Sent:** Thu, 12 Oct 2017 13:36:19 +0000  
**To:** (b)(6); Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Khabbaz, Rima (CDC/OID/NCEZID); Mahon, Barbara (CDC/OID/NCIRD); (b)(6)  
**Subject:** RE: Meningococcal SBA Testing at CDC?

Hi all,

Kent, thanks for the introduction. Would be happy to discuss in more detail. Perhaps Michael can set up a TC with our project team?

Separately, I had reached out to Sandy Steiner who connected me with Shankar Rajam on this topic. I assume Shankar works in Barbara's division?

JH

-----Original Message-----

**From:** Kester, Kent /US  
**Sent:** Tuesday, October 10, 2017 2:58 PM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Khabbaz, Rima (CDC/OID/NCEZID); Mahon, Barbara (CDC/OID/NCIRD); Heinrichs, Jon /US  
**Subject:** RE: Meningococcal SBA Testing at CDC?

Thanks, Nancy. I've copied my colleague Jon Heinrichs who is interested in this aspect.

Best regards,

Kent Kester

Kent E. Kester, MD  
Vice President and Head, Translational Science & Biomarkers Sanofi Pasteur  
**Phone:** (b)(6)  
(b)(6)

-----Original Message-----

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [<mailto:nar5@cdc.gov>]  
**Sent:** Tuesday, October 10, 2017 2:02 PM  
**To:** Kester, Kent /US  
**Cc:** Khabbaz, Rima (CDC/OID/NCEZID); Mahon, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: Meningococcal SBA Testing at CDC?

Kent,

CDC has a long history of doing SBA, including in the context of CRADA's with several vaccine manufacturers. More recently, we let our capacity lapse, but we are actually now in the process of getting SBA for mening up and running. We'd love to talk to you about your needs and what CDC is doing. Suggest you contact Barbara Mahon, who is the division director over that laboratory.

Nancy

Nancy Messonnier, MD  
Director  
National Center for Immunization and Respiratory Diseases OI, CDC

-----Original Message-----

From: Khabbaz, Rima (CDC/OID/NCEZID)  
Sent: Friday, October 6, 2017 3:07 PM  
To: (b)(6)  
Cc: Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>  
Subject: Re: Meningococcal SBA Testing at CDC?

Hello Kent,  
Referring you to Nancy who will know.  
Rima  
Sent from my BlackBerry 10 smartphone.

Original Message  
From: (b)(6)  
Sent: Friday, October 6, 2017 11:50 AM  
To: Khabbaz, Rima (CDC/OID/NCEZID)  
Subject: Meningococcal SBA Testing at CDC?

Dear Rima--

Is there anyone at the CDC who currently does meningococcal SBA testing?

Kent

\*\*\*\*\*

Cette communication (y compris les pieces jointes) est reservee a l'usage exclusif du destinataire (des destinataires) et peut contenir des informations privilegiees, confidentielles, exemptees de divulgation selon la loi ou protegees par les droits d'auteur. Si vous n'etes pas un destinataire, toute utilisation, divulgation, distribution, reproduction, examen ou copie (totale ou partielle) est non-autorisee et peut etre illegale. Tout message electronique est susceptible d'alteration et son integrite ne peut etre assuree. Sanofi Pasteur decline toute responsabilite au titre de ce message s'il a ete modifie ou falsifie. Si vous n'etes pas destinataire de ce message, merci de le detruire immediatement et d'avertir l'expediteur de l'erreur de distribution et de la destruction du message. Merci.  
This transmission (including any attachments) is intended solely for the use of the addressee(s) and may contain confidential information including trade secrets which are privileged, confidential, exempt from disclosure under applicable law and/or subject to copyright. If you are not an intended recipient, any use, disclosure, distribution, reproduction, review or copying (either whole or partial) is unauthorized and may be unlawful. E-mails are susceptible to alteration and their integrity cannot be guaranteed. Sanofi Pasteur shall not be liable for this e-mail if modified or falsified. If you are not the intended recipient of this e-mail, please delete it immediately from your system and notify the sender of the wrong delivery and the mail deletion. Thank you.

\*\*\*\*\*

\*\*\*\*\*

Cette communication (y compris les pieces jointes) est reservee a l'usage exclusif du destinataire (des destinataires) et peut contenir des informations privilegiees, confidentielles, exemptees de divulgation selon la loi ou protegees par les droits d'auteur. Si vous n'etes pas un destinataire, toute utilisation, divulgation, distribution, reproduction, examen ou copie (totale ou partielle) est non-autorisee et peut etre illegale. Tout message electronique est susceptible d'alteration et son integrite ne peut etre assuree. Sanofi Pasteur decline toute responsabilite au titre de ce message s'il a ete modifie ou falsifie. Si vous n'etes pas destinataire de ce message, merci de le detruire immediatement et d'avertir l'expediteur de l'erreur de distribution et de la destruction du message. Merci.  
This transmission (including any attachments) is intended solely for the use of the addressee(s) and may contain

confidential information including trade secrets which are privileged, confidential, exempt from disclosure under applicable law and/or subject to copyright. If you are not an intended recipient, any use, disclosure, distribution, reproduction, review or copying (either whole or partial) is unauthorized and may be unlawful. E-mails are susceptible to alteration and their integrity cannot be guaranteed. Sanofi Pasteur shall not be liable for this e-mail if modified or falsified. If you are not the intended recipient of this e-mail, please delete it immediately from your system and notify the sender of the wrong delivery and the mail deletion. Thank you.

\*\*\*\*\*

**From:** York, Laura  
**Sent:** Wed, 1 Nov 2017 18:25:14 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** RE: didn't note

Yes, you were busy!  
Maybe Feb.

Laura

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [mailto:nar5@cdc.gov]  
**Sent:** Wednesday, November 1, 2017 1:57 PM  
**To:** York, Laura  
**Subject:** [EXTERNAL] RE: didn't note

Thanks. I did retire from the public health service after 20 years in uniform. I was rehired by CDC and am now a civil servant.  
Sorry we didn't get to chat at all last week.  
Nancy

---

**From:** York, Laura [mailto:(b)(6)]  
**Sent:** Wednesday, November 1, 2017 1:36 PM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>  
**Subject:** didn't note

Hi Nancy

I hadn't noted, but Luis pointed out that you were not in uniform while at the ACIP table. This means I should be congratulating you for 25 years, correct? Anyway - here's to your continued success in the role as a civilian!

Kind regards  
Laura

**Laura J. York, PhD**  
VP, Global Meningococcal Vaccines,  
Medical Development and Scientific/Clinical Affairs

500 Arcola Road, Collegeville, PA, USA 19426  
Vaccines | Pfizer Inc.

(b)(6)

**From:** (b)(6)  
**Sent:** Wed, 17 Jan 2018 04:31:45 +0000  
**To:** Cohn, Amanda (CDC/OID/NCIRD); Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** RE: Re:

Certainly –  
Thank you for your response.

Julian

---

**From:** Cohn, Amanda (CDC/OID/NCIRD) [mailto:[anc0@cdc.gov](mailto:anc0@cdc.gov)]  
**Sent:** Tuesday, January 16, 2018 9:48 PM  
**To:** Ritchey, Julian /US; Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** [EXTERNAL] Re:

Hi Julian,

Thanks for reaching out. I am sorry we did not respond earlier, we are going to coordinate with some folks here and I will be in touch in the next few days.

Best,  
Amanda

---

**From:** (b)(6) <(b)(6)>  
**Date:** January 15, 2018 at 12:13:29 AM EST  
**To:** Cohn, Amanda (CDC/OID/NCIRD) <[anc0@cdc.gov](mailto:anc0@cdc.gov)>, Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Subject:** Fwd:

> Dear Nancy and Amanda -  
> I hope this finds you both well and warm amid the cool spell we all seem to be having right now.  
>  
> It probably comes as no surprise that we are watching anxiously the unfolding events around influenza this season given the trends for severe and prevalent disease. The CDC flu brief conference call on Friday gave a very nice update of the latest measures which I am hopeful will help calm some less well-founded fears out there. (b)(4)

(b)(4)

>  
> Would it be possible for us to have a brief chat on the phone sometime this week to touch base and think ahead on



this issue. I appreciate understanding what you are hearing, discuss some of the scenarios we are watching, and consider any coordination among CDC, companies and organizations that would be constructive and appropriate.

>

> Be well and I look forward to being in touch -

> Julian Ritchey

> Sanofi Pasteur

>

**From:** Krmpotich, Jane C  
**Sent:** Thu, 8 Feb 2018 22:12:29 +0000  
**To:** Painter, Elizabeth (CDC/OID/NCIRD) (CTR); Ogden, Lydia; Sterk, Nancy; Messonnier, Nancy (CDC/OID/NCIRD); Cozart, Barbara (CDC/OID/NCIRD); Pope, Kristin (CDC/OID/NCIRD)  
**Subject:** RE: Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018

Thank you Eli.

I'll arrange Dr. Gerberding's travel to Atlanta. From there she travels to Europe so we'll take care of that as well. If you can arrange her hotel accommodations for the evening of May 6 and her ground transportation to/from the airport, that would be helpful. More on those details later.

Best regards,  
Jane

**Jane Krmpotich**

Office of Julie L. Gerberding, M.D., M.P.H.

Executive Vice President & Chief Patient Officer

Strategic Communications, Global Public Policy, and Population Health

Merck & Co., Inc. | 351 N. Sumneytown Pike (UG4CD-04), North Wales, PA 19454 | Phone:

(b)(6)



**From:** Painter, Elizabeth (CDC/OID/NCIRD) (CTR) [mailto:ocv3@cdc.gov]  
**Sent:** Thursday, February 08, 2018 4:51 PM  
**To:** Ogden, Lydia; Sterk, Nancy; Messonnier, Nancy (CDC/OID/NCIRD); Cozart, Barbara (CDC/OID/NCIRD); Pope, Kristin (CDC/OID/NCIRD)  
**Cc:** Krmpotich, Jane C  
**Subject:** RE: Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018

**EXTERNAL EMAIL** – Use caution with any links or file attachments.

Dear Jane and Dr. Ogden,

Thanks so much for the emails. We are thrilled that Dr. Gerberding will be able to participate in the symposium. I'll be in touch soon with more details about both the panel and travel arrangements- in the meantime, feel free to contact me if you have questions.

All the best,  
Eli

Elizabeth (Eli) Painter, PhD, MIM/MBA, CFA  
CNI  
Policy Team, Influenza Division

CDC/ National Center for Immunization and Respiratory Diseases

Phone: (b)(6)  
Blackberry: (b)(6)

---

**From:** Ogden, Lydia (b)(6)  
**Sent:** Thursday, February 8, 2018 4:41 PM  
**To:** Sterk, Nancy <nsterk@emory.edu>; Painter, Elizabeth (CDC/OID/NCIRD) (CTR) <ocv3@cdc.gov>; Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>; Cozart, Barbara (CDC/OID/NCIRD) <wjn4@cdc.gov>; Pope, Kristin (CDC/OID/NCIRD) <kfp7@cdc.gov>  
**Cc:** Krmpotich, Jane C (b)(6)  
**Subject:** RE: Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018"

Dear CDC and Emory Colleagues: Thanks for including Julie in this exciting program. Please feel free to reach to me with any suggestions about key messages you'd like her to deliver or to coordinate with other panelists, etc. All the best. Y'all have been in our thoughts. LO

Lydia L. Ogden, PhD, MPP  
Associate Vice President Global Enterprise Policy  
Merck  
Voice and text: (b)(6)  
Email: (b)(6)  
Executive Assistant: Jackie Cochran  
Email: (b)(6)  
Voice/text: (b)(6)  
Desk: (b)(6)



---

**From:** Krmpotich, Jane C  
**Sent:** Thursday, February 08, 2018 4:33 PM  
**To:** Sterk, Nancy  
**Cc:** Painter, Elizabeth (CDC/OID/NCIRD) (CTR); Ogden, Lydia; Messonnier, Nancy (CDC/OID/NCIRD); Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018"

Hi Nancy and Dr. Painter,

I am pleased to let you know that Dr. Julie Gerberding looks forward to participating in this program on May 7 in Atlanta. I've noted the details on her calendar and will look for additional information regarding the event as the date approaches. Thank you.

Best regards,  
Jane

**Jane Krmpotich**

Office of Julie L. Gerberding, M.D., M.P.H.

Executive Vice President & Chief Patient Officer

Strategic Communications, Global Public Policy, and Population Health

Merck & Co., Inc. | 351 N. Sumneytown Pike (UG4CD-04), North Wales, PA 19454 | Phone: (b)(6)



---

**From:** Sterk, Nancy [<mailto:nsterk@emory.edu>]

**Sent:** Monday, February 05, 2018 1:42 PM

**To:** Gerberding, Julie

**Cc:** Painter, Elizabeth (CDC/OID/NCIRD) (CTR); Krmpotich, Jane C; Ogden, Lydia

**Subject:** Invitation to Participate - "100 Years of Influenza Pandemics and Practice: 1918-2018"

**EXTERNAL EMAIL** – Use caution with any links or file attachments.

Good afternoon - I'm writing on behalf of Dr. Jim Curran to invite you to participate in the "100 years of Influenza Pandemics and Practice: 1918-2018" one-day symposium on Monday, May 7, 2018 in Atlanta, GA. The event is a partnership between the Rollins School of Public Health and the Centers for Disease Control and Prevention.

Attached to this email is the letter of invitation from Dr. Curran. Please respond directly to Dr. Eli Painter (copied on this email) with your availability.

We look forward to hearing back from you.

**Nancy**

Nancy Sterk

Executive Administrative Assistant to James W. Curran, MD, MPH / James W. Curran Dean of Public

Health / Rollins School of Public Health, Emory University / 1518 Clifton Road, NE, Suite 8000E /

Mailstop:1518-002-8BB / Atlanta, GA 30322 PH:404.727.8720 / CELL (b)(6) / FAX:404.712.8879 /

email: [nsterk@emory.edu](mailto:nsterk@emory.edu) / web: <http://www.sph.emory.edu>

---



This e-mail message (including any attachments) is for the sole use of the intended recipient(s) and may contain confidential and privileged information. If the reader of this message is not the intended recipient, you are hereby notified that any dissemination, distribution or copying of this message (including any attachments) is strictly prohibited.

If you have received this message in error, please contact the sender by reply e-mail message and destroy all copies of the original message (including attachments).

**Notice:** This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**Notice:** This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.



**From:** Jodar, Luis  
**Sent:** Tue, 10 Apr 2018 15:16:12 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** Re: [EXTERNAL] RE: chat

Hi Nancy,

No worries.

(b)(6)

(b)(6) Barbara, Raul and I had a good conversation and I understand from Raul that a face to face meeting with CDC is scheduled on April 27th. I am flying to Japan now and from there to ISPPD, where I will likely see Cindy and Tamara. I think we can wait for the meeting on the 27th to occur and if there are any remaining issues then you and I can talk. Does it sound reasonable? In any event you can always give me a call at (b)(6)  
Luis

Sent from my iPhone

On Apr 9, 2018, at 16:07, Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)> wrote:

Hi Luis,

(b)(6)

I understand from Barbara that your conversation went well; I hope you agree. I'm happy to touch base this week if you'd still like to.

Nancy

**From:** Jodar, Luis <(b)(6)>  
**Sent:** Monday, April 2, 2018 1:57 PM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Subject:** chat

Hi Nancy- Hope all is well. I talked to Peter. As you know, Raul and I are talking to Barbara this afternoon. Perhaps you and I can briefly chat at the end of the week? Please let me know and also a good time and phone number. Let's keep it informal. Cheers, Luis

**From:** (b)(6)  
**Sent:** Thu, 12 Apr 2018 20:33:37 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Cozart, Barbara (CDC/OID/NCIRD) (b)(6)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation

Thank you Nancy – this is great news – and we now have a terrific line-up!

Best,  
Karen

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [mailto:nar5@cdc.gov]  
**Sent:** Thursday, April 12, 2018 4:22 PM  
**To:** Chandross, Karen /US (b)(6)  
**Cc:** Cozart, Barbara (CDC/OID/NCIRD) <wjn4@cdc.gov>  
**Subject:** [EXTERNAL] RE: AAAS 2019 -- Universal flu vaccine proposal invitation

I'd be happy to.

*Nancy Messonnier, MD  
Director  
National Center for Immunization and Respiratory Diseases  
OID, CDC  
1600 Clifton Road, MS A-27  
Atlanta, GA 30333  
404 639 4734*

---

**From:** (b)(6)  
**Sent:** Thursday, April 12, 2018 11:03 AM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>  
**Cc:** (b)(6)  
**Subject:** FW: AAAS 2019 -- Universal flu vaccine proposal invitation  
**Importance:** High

Dear Dr. Messonnier,

I'm reaching out to invite you to participate in a session that Gary Nabel and I are proposing for the 2019 AAAS meeting (February 14-18) in Washington, DC – and for which Anne Schuchat highly recommended you as a speaker.

In line with AAAS's interest in topics with broad appeal and relevancy, we would like to submit a proposal for a 90-min symposium (<https://aaas.confex.com/aaas/2019/symp90/cfp.cgi>) on "The quest for a universal flu vaccine."

The theme for the 2019 meeting is "*Science Transcending Boundaries*," which offers an opportunity to bridge the gap between scholar and practitioner and leverage expertise from different disciplines to highlight the greatest challenges and most promising solutions to achieving an impactful solution.

For the session format, 3 speakers are asked to give presentations (~20 minutes each), followed by a ~30 minute Q&A period with the audience- moderated by David Baltimore.

Please see the proposal below for your consideration and comments. There is no guarantee that it will be selected but having a relevant topic and confirmed speakers helps and your expertise, experience and perspective would be highly valued.

We look forward to your decision, noting that this is time sensitive with a submission deadline of April 19<sup>th</sup>.

If you agree, then please reply with your full contact information—that includes your CDC affiliation.

Best regards,  
Karen

**Karen CHANDROSS, PhD**

**Senior Director, Strategic Initiatives & Scientific Relations**  
Sanofi R&D

TEL: (b)(6) | CELL: (b)(6) | (b)(6)

### **The quest for a universal flu vaccine**

According to the World Health Organization, seasonal influenza epidemics cause 3 to 5 million severe cases and 300,000 to 500,000 deaths globally each year. In the United States alone, there are 140,000 to 710,000 influenza-related hospitalizations and 12,000 to 56,000 deaths each year, with the highest burden of disease affecting the very young, the very old, and people with coexisting medical conditions. The most recent 2017/2018 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

**Moderator:** David Baltimore, PhD, Caltech (*confirmed*)

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO (*confirmed*)

Anthony Fauci, MD, NIAID Director (*confirmed*)

Nancy Messonnier, MD, CDC NCIRD Director

**Proposed by:** Gary Nabel, MD, PhD & Karen Chandross, PhD, Sanofi R&D

**From:** (b)(6)  
**Sent:** Wed, 18 Apr 2018 16:53:58 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Dr. Messonnier, please send title & 2-3 sentence description today

... how is this:

How can we reduce the burden of influenza until the promise of a “universal” flu vaccine is realized and what can we do now to lay the ground-work for its acceptance? As we track domestic and international surveillance trends and learn more about how the influenza virus works and our response to it, we have to improve our current vaccines and evaluate if different types are more beneficial. Data shows that flu vaccine coverage is directly linked to how well the vaccine works. Working to ensure the current vaccines are effective and safe can pave the way for acceptance of a universal vaccine.

---

**From:** Chandross, Karen /US  
**Sent:** Wednesday, April 18, 2018 10:56 AM  
**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>  
**Cc:** Cozart, Barbara (CDC/OID/NCIRD) <wjn4@cdc.gov>  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Dr. Messonnier, please send title & 2-3 sentence description today

Great title – thank you for your quick response!

I just tried to upload to the AAAS system but they are limiting the summary to 500 characters – if you could shorten (you are currently at 616).

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [<mailto:nar5@cdc.gov>]  
**Sent:** Wednesday, April 18, 2018 10:38 AM  
**To:** Chandross, Karen /US <(b)(6)>  
**Cc:** Cozart, Barbara (CDC/OID/NCIRD) <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>  
**Subject:** [EXTERNAL] Re: AAAS 2019 -- Universal flu vaccine proposal -- Dr. Messonnier, please send title & 2-3 sentence description today

Hit me with your best shot: before and after a universal flu vaccine

While the promise of a universal influenza vaccine may be years in the future, how can we reduce the burden of influenza until a universal flu vaccine is developed and what can we do now to lay the ground work for acceptance of a universal flu vaccine? As we track domestic and international surveillance trends and learn more about how the influenza virus works and our response to it, we have to improve our current vaccines and evaluate if different types of flu vaccine are more beneficial. Data tells us that flu vaccine coverage is directly



linked to how well the vaccine works. Working to ensure the current vaccines are effective and safe before we have a universal vaccine can pave the way for acceptance when we have a universal flu vaccine.

On Apr 18, 2018, at 9:37 AM, "[REDACTED]" <[REDACTED]> wrote:

Dear Nancy, if you would please send me your title and a few sentences today so that we may submit our proposal by tomorrow's deadline.

Thank you.

Best,  
Karen

---

**From:** Conrad, Patricia (NIH/NIAID) [E] <<mailto:conradpa@niaid.nih.gov>>  
**Sent:** Wednesday, April 18, 2018 8:58 AM  
**To:** Nabel, Gary /US <[REDACTED]>; Chandross, Karen /US <[REDACTED]>; Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@CDC.GOV](mailto:nar5@CDC.GOV)>  
**Cc:** Baltimore, David <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; Wei, Ronnie /US <[REDACTED]>; Travayiakis, Carol /U <[REDACTED]>; Cozart, Barbara (CDC/OID/NCIRD) <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation -- all proposed participants confirmed -- please send title & 2-3 sentence description

Karen:

Attached is Dr. Fauci's title and abstract.

Thank you,  
-patty

Patricia L. Conrad  
Special Assistant to the Director

Disclaimer:  
The information in this e-mail and any of its attachments is confidential and may contain sensitive information. It should not be used by anyone who is not the original intended recipient. If you have received this e-mail in error please inform the sender and delete it from your mailbox or any other storage devices. National Institute of Allergy and Infectious Diseases (NIAID) shall not accept liability for any statement made that are sender's own and not expressly made on behalf of the NIAID by one of its representatives.

---

**From:** [REDACTED] <[\[REDACTED\]](mailto:[REDACTED])>  
**Sent:** Monday, April 16, 2018 2:29 PM  
**To:** [REDACTED]; Messonnier, Nancy (CDC/OID/NCIRD)



<[nar5@CDC.GOV](mailto:nar5@CDC.GOV)>; Fauci, Anthony (NIH/NIAID) [E] (b)(6)  
**Cc:** Baltimore, David <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; (b)(6)  
(b)(6) Conrad, Patricia (NIH/NIAID) [E] <[conradpa@niaid.nih.gov](mailto:conradpa@niaid.nih.gov)>;  
Cozart, Barbara (CDC/OID/NCIRD) <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation -- all proposed participants confirmed -- please send title & 2-3 sentence description

Hi Karen,

Here is a first pass proposal.

Title: Rational Design and Development of Universal Influenza Vaccines

This talk will cover the alternative paths to improved influenza vaccines. Different potential approaches to a broadly protective antibody will be highlighted. Major scientific challenges and opportunities based on influenza biology and the human immune response will be discussed. Finally, considerations for product development will be reviewed, including clinical testing, regulatory, and manufacturing issues, as well as opportunities to advance through public-private partnerships.

I will adjust my presentation to complement Tony and Nancy's talks.

Best  
Gary

---

**From:** Chandross, Karen /US  
**Sent:** Monday, April 16, 2018 11:16 AM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD) (b)(6); Nabel, Gary /US  
**Cc:** Baltimore, David; Wei, Ronnie /US; Travayiakis, Carol /US; Conrad, Patricia (NIH/NIAID) [E]; Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation -- all proposed participants confirmed -- please send title & 2-3 sentence description  
**Importance:** High

Dear All – thank you for agreeing to participate in a proposed 2019 AAAS session, which focuses on addressing *The quest for a universal flu vaccine*.

We are very excited to have a great line up and, if selected, David Baltimore has kindly agreed to serve as moderator.

Speakers:

Gary Nabel, MD, PhD, Sanofi CSO  
Anthony Fauci, MD, NIH-NIAID Director  
Nancy Messonnier, MD, CDC-NCIRD Director

Keeping in mind the April 19<sup>th</sup> submission deadline, for our speakers, I must submit a 1) a **title for your talk** and 2) **up to 3 short sentences that describes your focus**-- if you would send this to me at your earlier convenience.

Please note that we would plan to have short talks followed by a longer panel discussion that also includes engaging the audience.

All the best,  
Karen

**Info:**

1. 2019 AAAS meeting (February 14-18) in Washington, DC.
2. In line with AAAS's interest in topics with broad appeal and relevancy, we are submitting a proposal for a 90-min symposium (<https://aaas.confex.com/aaas/2019/symp90/cfp.cgi>) on "*The quest for a universal flu vaccine.*"
3. Theme is "*Science Transcending Boundaries,*" which offers an opportunity to bridge the gap between scholar and practitioner and leverage expertise from different disciplines to highlight the greatest challenges and most promising solutions to achieving an impactful solution.
4. For the session format, 3 speakers are asked to give presentations (~20 minutes each), followed by a ~30 minute Q&A period with the audience.

**The quest for a universal flu vaccine**

According to the World Health Organization, seasonal influenza epidemics cause 3 to 5 million severe cases and 300,000 to 500,000 deaths globally each year. In the United States alone, there are 140,000 to 710,000 influenza-related hospitalizations and 12,000 to 56,000 deaths each year, with the highest burden of disease affecting the very young, the very old, and people with coexisting medical conditions. The most recent 2017/2018 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal

flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

**Moderator:** David Baltimore, PhD

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

**Organizer:** Karen Chandross, PhD, Sanofi R&D

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL: (b)(6) | (b)(6)

**From:** (b)(6)  
**Sent:** Wed, 7 Mar 2018 13:31:29 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** Phil Hosbach Retiring

Hi Nancy –  
I hope this finds you well and amid a flu season improving at least somewhat!

(b)(6)  
(b)(6) We have been looking for an opportunity to recognize Phil and one has come together quickly next week via a meeting where a number of French and American colleagues will be together. For this, I am trying to gather comments, and ideally, letters from people we know have been special to Phil and with whom I know he's worked closely. As we've discussed and I can certainly attest from my years with Phil, he has great admiration for you and your work. You have both shared a number of challenges - and good times too - over the years.

Would you be so kind as to write a brief letter to Phil that we can cite in our celebration (or "memorial service"! ) Ideally, a pdf of your note on letterhead would be great as we would like to have these bound into a book.

The occasion is next Tues, so would it be possible to secure a note from you by this coming Monday, 3/12?

Thank you, Nancy. I know he will appreciate this and I certainly do too.

Regards,  
Julian

**From:** (b)(6)  
**Sent:** Sun, 28 Jan 2018 21:07:11 +0000  
**To:** Cohn, Amanda (CDC/DDID/NCIRD/OD); Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** RE: Re:

Hi Amanda-

I realized I did not respond to your note.

I see that BIO has set-up a call. I'm in Geneva but will do my best to dial in.

Look forward to your thoughts on how you are seeing the flu see unfold.

Julian

---

**From:** Cohn, Amanda (CDC/OID/NCIRD) [mailto:[anc0@cdc.gov](mailto:anc0@cdc.gov)]  
**Sent:** Tuesday, January 23, 2018 1:27 PM  
**To:** Ritchey, Julian /US; Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** [EXTERNAL] RE: Re:

Julian,

Sorry for the delayed response! We agree that this is an important discussion for us to have with vaccine companies. We would like to coordinate through BIO to have a call that focuses on this issue and gives companies an opportunity to ask questions and give feedback. After the call, if you have anything you would like to discuss in private we can arrange that, but our goal is to be consistently transparent when possible, and this discussion lends itself well to that approach.

Thanks!

Amanda

---

**From:** (b)(6) [mailto:(b)(6)]  
**Sent:** Tuesday, January 23, 2018 12:15 PM  
**To:** Cohn, Amanda (CDC/OID/NCIRD) <[anc0@cdc.gov](mailto:anc0@cdc.gov)>; Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Subject:** RE: Re:

Dear both –

I hope that operations are regaining some normalcy with the return of funding and the shutdown was not too burdensome to you and your teams.

Just checking in on the note below to see if/when we might connect.

Obviously I respect the prioritization challenges you might be facing with the shutdown, so please don't read this as being pushy!

Julian



---

**From:** Cohn, Amanda (CDC/OID/NCIRD) [<mailto:anc0@cdc.gov>]  
**Sent:** Tuesday, January 16, 2018 9:48 PM  
**To:** Ritchey, Julian /US; Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** [EXTERNAL] Re:

Hi Julian,

Thanks for reaching out. I am sorry we did not respond earlier, we are going to coordinate with some folks here and I will be in touch in the next few days.

Best,  
Amanda

---

**From:** (b)(6) <(b)(6)>  
**Date:** January 15, 2018 at 12:13:29 AM EST  
**To:** Cohn, Amanda (CDC/OID/NCIRD) <[anc0@cdc.gov](mailto:anc0@cdc.gov)>, Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Subject:** Fwd:

> Dear Nancy and Amanda -  
> I hope this finds you both well and warm amid the cool spell we all seem to be having right now.  
>  
> It probably comes as no surprise that we are watching anxiously the unfolding events around influenza this season given the trends for severe and prevalent disease. The CDC flu brief conference call on Friday gave a very nice update of the latest measures which I am hopeful will help calm some less well-founded fears out there. (b)(4)

(b)(4)

> Would it be possible for us to have a brief chat on the phone sometime this week to touch base and think ahead on this issue. I appreciate understanding what you are hearing, discuss some of the scenarios we are watching, and consider any coordination among CDC, companies and organizations that would be constructive and appropriate.

> Be well and I look forward to being in touch -

> Julian Ritchey  
> Sanofi Pasteur

>



**From:** (b)(6)  
**Sent:** Wed, 18 Apr 2018 20:44:45 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Cozart, Barbara (CDC/DDID/NCIRD/OD) (b)(6) Conrad, Patricia (NIH/NIAID) [E]; Gary.Nabel@sanofi.com; baltimo@caltech.edu  
**Cc:** (b)(6)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- final submission for your review  
**Attachments:** AAAS Flu Vaccine Proposal-Submission.docx

Thank you for your quick response and contributions to the *Quest for a universal flu vaccine* AAAS proposal.

Attached please find our submission package.

I'll hold off hitting the "submit" button until tomorrow morning to allow time for final comments - and will share the decision, once available.

Thank you.  
Karen

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL (b)(6) CELL (b)(6) (b)(6)

**From:** Chandross, Karen /US  
**Sent:** Monday, April 16, 2018 11:16 AM  
**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; (b)(6)  
(b)(6) Nabel, Gary /US <(b)(6)>  
**Cc:** 'Baltimore, David' <baltimo@caltech.edu>; Wei, Ronnie /US (b)(6)  
Travayiakis, Carol /US <(b)(6)>; 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; Cozart, Barbara (CDC/OID/NCIRD) <wjn4@cdc.gov>  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation -- all proposed participants confirmed -- please send title & 2-3 sentence description  
**Importance:** High

Dear All – thank you for agreeing to participate in a proposed 2019 AAAS session, which focuses on addressing *The quest for a universal flu vaccine*.

We are very excited to have a great line up and, if selected, David Baltimore has kindly agreed to serve as moderator.

**Speakers:**  
Gary Nabel, MD, PhD, Sanofi CSO  
Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

Keeping in mind the April 19<sup>th</sup> submission deadline, for our speakers, I must submit a 1) a **title for your talk** and 2) **up to 3 short sentences that describes your focus--** if you would send this to me at your earlier convenience.

Please note that we would plan to have short talks followed by a longer panel discussion that also includes engaging the audience.

All the best,  
Karen

**Info:**

1. 2019 AAAS meeting (February 14-18) in Washington, DC.
2. In line with AAAS's interest in topics with broad appeal and relevancy, we are submitting a proposal for a 90-min symposium (<https://aaas.confex.com/aaas/2019/symp90/cfp.cgi>) on "*The quest for a universal flu vaccine.*"
3. Theme is "*Science Transcending Boundaries,*" which offers an opportunity to bridge the gap between scholar and practitioner and leverage expertise from different disciplines to highlight the greatest challenges and most promising solutions to achieving an impactful solution.
4. For the session format, 3 speakers are asked to give presentations (~20 minutes each), followed by a ~30 minute Q&A period with the audience.

**The quest for a universal flu vaccine**

According to the World Health Organization, seasonal influenza epidemics cause 3 to 5 million severe cases and 300,000 to 500,000 deaths globally each year. In the United States alone, there are 140,000 to 710,000 influenza-related hospitalizations and 12,000 to 56,000 deaths each year, with the highest burden of disease affecting the very young, the very old, and people with coexisting medical conditions. The most recent 2017/2018 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

**Moderator:** David Baltimore, PhD

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

**Organizer:** Karen Chandross, PhD, Sanofi R&D

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) | CELL: (b)(6) | (b)(6)

## **The quest for a universal flu vaccine**

Submitter's Email: (b)(6)

### **Session Type:**

90 Minute Symposium Format

### **Session Description:**

Seasonal influenza epidemics cause 3-5 million severe cases and up to 500K deaths globally each year. In the US alone, there are 140K-710K influenza-related hospitalizations and 12K-56K deaths each year, with the highest burden of disease affecting the very young, the very old and people with coexisting medical conditions. The most recent 2017-18 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

### **Categories:**

1. Health and Pharmaceutical Science
2. Global Perspectives and Issues

**Section Member Affiliation:** Pharmaceutical Sciences (S)

### **Relevance to Theme or Special Relevance to the Audience:**

Bridging the gap between scholar and practitioner and leverage expertise from different disciplines: Pharma (private sector), National Institutes of Health (NIH), and the Centers for Disease Control and Prevention, and National Center for Immunization and Respiratory Diseases (CDC-NCIRD), to span the breadth from innovative research to product development and global access, discuss the greatest challenges and most promising approaches, and collaborative opportunities aimed at achieving an impactful, timely solution.

### **Disciplinary Sections Consulted?**

Yes

### **If so, which sections were consulted?**

- Pharmaceutical Sciences (S)

### **Anything to disclose?**

No

### **Diversity Statement:**

Well-balanced, cross disciplinary session with senior level professional participants from both the private (Pharma) and public (NIH, CDC) sectors, coming from different cultural backgrounds and with the inclusion of women as key contributors (session organizer, speaker).

### **Sections:**

- GENERAL INTEREST IN SCIENCE AND ENGINEERING
- MEDICAL SCIENCES
- PHARMACEUTICAL SCIENCES

**Keywords:** biomedical research (clinical), biomedical research (preclinical), disease prevention, global and public health and infectious disease

**Moderator**

David Baltimore, PhD  
President Emeritus; Robert Andrews Millikan Professor of Biology  
Caltech  
1200 East California Blvd  
Mail Code 147-75  
Pasadena, CA  
USA  
**Phone Number:** (b)(6)  
**Email:** baltimo@caltech.edu

**Organizer**

Karen Chandross, PhD  
Senior Director, R&D  
Sanofi  
55 Corporate Drive  
Bridgewater, NJ  
USA  
**Phone Number:** (b)(6)  
**Email:** (b)(6)

---

**Speaker**

Gary J. Nabel, MD, PhD  
Chief Scientific Officer  
Sanofi  
640 Memorial Drive  
Room 5951A  
Cambridge, MA  
USA  
**Phone Number:** (b)(6)  
**Email:** (b)(6)

**Title:** Rational Design and Development of Universal Influenza Vaccines

**Talk Description:** This talk will cover the alternative paths to improved influenza vaccines. Different potential approaches to a broadly protective antibody will be highlighted. Major scientific challenges and opportunities based on influenza biology and the human immune response will be discussed. Finally, considerations for product development will be reviewed, including clinical testing, regulatory, and manufacturing issues, as well as opportunities to advance through public-private partnerships.

**Status:** Confirmed

---

**Speaker**

Anthony Fauci, MD  
Director  
NIH, National Institute of Allergy and Infectious Disease (NIAID)  
31 Center Drive  
Building 31, Room 7A03  
Bethesda, MD  
USA  
**Phone Number:** (b)(6)  
**Email:** (b)(6)

**Title:** Chasing Influenza: The Need for a Universal Influenza Vaccine

**Talk Description:** The cornerstone of both seasonal and pandemic influenza prevention and control is strain-specific vaccination. This approach is suboptimal for three main reasons: 1) current seasonal influenza vaccines are not consistently effective 2) influenza pandemics do occur and response after the fact is not effective 3) chasing after potential pandemic outbreaks (pre-pandemic) viruses is costly and ineffective. We are working to improve influenza vaccines with an eye toward a universal influenza vaccine that would protect against both seasonal and pandemic viruses. To achieve this goal, we must overcome two major challenges: improving production strategies for influenza

vaccines and advancing from strain-specific vaccines to universal strain coverage.

**Status:** Confirmed

---

**Speaker**

Nancy Messonnier, MD

Director

National Center for Immunization and Respiratory Diseases, CDC-OID

1600 Clifton Road

MS A-27

Atlanta, GA

USA

**Phone Number:** 404.639.4734

**Email:** nar5@cdc.gov

**Title:** Hit Me With Your Best Shot: Before and After a Universal Flu Vaccine

**Talk Description:** While the promise of a universal flu vaccine may be years in the future, how can we reduce flu burden until one is developed and what ground work can we lay in advance? As we track domestic and international surveillance trends and learn more about how flu works and our response to it, we have to improve our current vaccines and evaluate if different types of vaccine are more beneficial. Data tells us that flu vaccine coverage is linked to how well the vaccine works. Working to ensure the current vaccines are effective and safe before we have a universal vaccine can pave the way for its acceptance.

**Status:** Confirmed



**From:** (b)(6)  
**Sent:** Tue, 11 Jul 2017 17:33:54 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD);Cohn, Amanda (CDC/OID/NCIRD)  
**Cc:** (b)(6)  
**Subject:** Protein Sciences Press Release  
**Attachments:** Protein Sciences PR v06072017 8h15CET FINAL.docx

Greeting Nancy and Amanda-

Attached a press release for the announcement we are making today regarding our bid to purchase Protein Sciences.

Fast-moving and early in the process, I wanted to be sure you were aware of this initial step, and address any questions you might have.

I'd welcome any thoughts you might have -  
Julian



## Sanofi to acquire Protein Sciences

*- Acquisition adds recombinant-based influenza vaccine to Sanofi Pasteur's portfolio -*

**Paris, France – July 11, 2017** - [Sanofi](#) announced today it will acquire Protein Sciences, a privately held vaccines biotechnology company based in Meriden, Connecticut in the United States. Under the terms of the agreement, Sanofi will make an upfront payment of \$650 million and pay up to \$100 million upon achievement of certain milestones.

Protein Sciences received approval from the US Food and Drug Administration (FDA) in October 2016 for their Flublok® Quadrivalent Influenza Vaccine (QIV). Flublok® is the only recombinant protein-based influenza vaccine approved by the FDA.

*"The acquisition of Protein Sciences will allow us to broaden our flu portfolio with the addition of a non-egg based vaccine,"* said David Loew, Sanofi Executive Vice President and Head of Sanofi Pasteur, Sanofi's vaccines division.

*"Protein Sciences was actively looking for an opportunity to grow its business, particularly in the US,"* said Manon M.J. Cox, President and Chief Executive Officer, Protein Sciences. *"As part of Sanofi Pasteur, we expect our Flublok® influenza vaccine to benefit from Sanofi Pasteur's expertise in the field of influenza vaccines."*

The acquisition, which has been unanimously approved by the board of directors of Protein Sciences and a majority of Protein Sciences shareholders, is expected to close in the third quarter of 2017, subject to customary regulatory approvals.

### About Protein Sciences

Protein Sciences is a privately held biotech company established in 1983 and headquartered in Meriden, CT. Protein Sciences' mission is to save lives and improve health through the creation of innovative vaccines and biopharmaceuticals.

### About Sanofi Pasteur

Sanofi Pasteur produces vaccines against seasonal influenza on its four sites: Swiftwater (Pennsylvania, United States), Val de Reuil (France), Ocoyoacac (Mexico City, Mexico) and Shenzhen (China).

### About Sanofi

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi is organized into five global business units: Diabetes and Cardiovascular, General Medicines and Emerging Markets, Sanofi Genzyme, Sanofi Pasteur and Consumer Healthcare. Sanofi is listed in Paris (EURONEXT: [SAN](#)) and in New York (NYSE: [SNY](#)).

### Sanofi Forward-Looking Statements

*This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking*

statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could effect the availability or commercial potential of such product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic conditions, the impact of cost containment initiatives and subsequent changes thereto, the average number of shares outstanding as well as those discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2016. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

---

## **Contacts:**

### **Media Relations**

Jack Cox

Tel. : +33 (0)1 53 77 46 46

[mr@sanofi.com](mailto:mr@sanofi.com)

### **Investor Relations**

George Grofik

Tel.: +33 (0)1 53 77 45 45

[ir@sanofi.com](mailto:ir@sanofi.com)

**From:** Draghia, Ruxandra  
**Sent:** Fri, 11 Aug 2017 16:23:15 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD); Cohn, Amanda (CDC/OID/NCIRD)  
**Cc:** Dooling, Kathleen L.  
(CDC/OID/NCIRD); nancy\_bennett@urmc.rochester.edu; Bresnitz, Eddy A.  
**Subject:** Herpes Zoster Vaccines Discussion, ACIP Meeting, June 21, 2017  
**Attachments:** CDC HZ 081117 letter.pdf

Dear Drs. Messonnier and Cohn,

Please see the attached letter for your consideration.

Thank you,

Ruxandra Draghia, MD, PhD  
Vice President  
Public Health & Scientific Affairs  
Global Vaccines

P: (b)(6)  
M: (b)(6)

Assistant: Judy Carroll (b)(6)

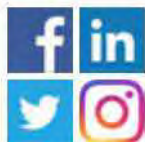
(b)(6)

[merck.com](http://merck.com)



**MERCK**

INVENTING FOR LIFE



Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error,

please notify us immediately by reply e-mail and then delete it from your system.

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

**From:** Fletcher, Mark  
**Sent:** Mon, 7 Sep 2015 06:15:31 +0000  
**To:** PEREA CARO, William Augusto; Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** York, Laura  
**Subject:** RE: MenC  
**Attachments:** SPC current (EN Common)- NeisVac-C - clean.doc

Dr William PERA CARO  
World Health Organization

Dear Dr Pera Caro

I am writing you on behalf of Pfizer Vaccines with respect to the Meningococcal Outbreak in Niger. Pfizer Vaccines would like your help in assessing the WHO's interest in a product donation of NeisVac-C to help protect against serogroup C disease.

We understand that although Serogroup C is the main serogroup reported in the outbreaks, cases of W-135 were also reported in Niger and Nigeria (according to WHO, 12% of positive isolates were due to serogroup W), and historically that serogroup A is the predominant serogroup in the Meningitis Belt.

We are also aware that the WHO, in conjunction with UNICEF and MSF, are trying to secure multivalent/ACWY vaccine (poly or conjugate) from different manufactures (multinational and smaller manufacturers) for this immediate situation (<http://www.who.int/csr/don/15-may-2015-niger/en/>). Nevertheless, because Serogroup C is the main serogroup reported in the outbreaks, Pfizer would be willing to donate NeisVac-C to the WHO.

Please note that NeisVac-C is indicated for active immunisation in children from 2 months of age, adolescents and adults, for the prevention of invasive disease caused by *Neisseria meningitidis* serogroup C. Please refer to attached SPC for additional details.

In addition, it

- Will be in the pre-filled syringe presentation,
- Will have a U.K. label, and
- Is not WHO pre-qualified

Pfizer is aware of the recent Meningitis outbreaks of serogroups C and W in Africa and the call from the ICG (International Coordinating Group for Vaccine Provision for Epidemic Meningitis Control) on vaccine manufacturers to increase meningitis C-containing vaccine production by 5 million doses before the 2016 meningitis season starts in January.

I wrote earlier to Dr Marie-Pierre Préziosi, but did not receive a response from her so far. Would the WHO be able to assist Pfizer with this possible donation? I am in Geneva this week, today through Wednesday, and if possible perhaps we can meet.

I thank you for your time, and look forward to hearing back from you soon.

All the best, Mark



Mark A. FLETCHER, M.D.

Senior Director, Global Medical Development and Scientific/Clinical  
Affairs

Regional Medical and Scientific Affairs Lead, Africa-Middle East-India &  
International Organizations Global Lead

Mobile: (b)(6)

(b)(6)

23-25, avenue du Dr Lannelongue, 2.111D

F-75668 Paris Cedex 14, France

Time zone: UTC +1h

Work week : Monday to Friday

---

**De :** PEREA CARO, William Augusto [mailto:pereaw@who.int]

**Envoyé :** mardi 1 septembre 2015 18:37

**À :** Messonnier, Nancy (CDC/OID/NCIRD)

**Cc :** Fletcher, Mark; York, Laura

**Objet :** RE: MenC

Hi Nancy,

Sounds like good news. Thanks for making the link.

Happy to discuss with Laura and Mark any time this week if OK with them

Best

William

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [mailto:nar5@cdc.gov]

**Sent:** 31 August 2015 18:39

**To:** PEREA CARO, William Augusto

**Cc:** (b)(6) York, Laura

**Subject:** MenC

Hi William,

By way of email, let me introduce you to Laura York and Mark Fletcher from Pfizer. Pfizer is interested in talking to WHO about potential use of NeisVac-C for outbreak control in the Meningitis Belt. Although it is not WHO prequalified, the vaccine has a long track record of safety and efficacy. Laura was not sure who to connect with in WHO and asked me to make the introductions. I think it great that Pfizer has reached out in this way and that they are interested in finding a way to make additional serogroup C vaccine available if needed in West Africa.

Thank you,

Nancy

*Nancy Messonnier, MD*  
*Deputy Director*  
*National Center for Immunization and Respiratory Diseases*  
*OID, CDC*

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

**From:** Feinberg, Mark  
**Sent:** Wed, 26 Nov 2014 15:02:02 -0500  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Widdowson, Marc-Alain (CDC/CGH/DGHP)  
**Subject:** Fwd: arranging for a call

Dear Nancy and Marc-Alan,

I hope you are both doing well.

I am looking forward to talking with you both and Anne next week to share perspectives and plans regarding Ebola vaccine development. Please let me know if there are specific issues you would like to discuss on the call. This will help me ensure that I have all of the relevant information for you, and if indicated, can arrange to have some of my Merck colleagues with specific technical expertise participate as well.

I hope you and yours have a great Thanksgiving holiday.

Best,

Mark

Mark Feinberg, MD, PhD

(b)(6)

Begin forwarded message:

**From:** "King, Dawn R. (CDC/OID/NCIRD) (CTR)" <[duk3@cdc.gov](mailto:duk3@cdc.gov)>  
**Date:** November 26, 2014 at 1:00:03 PM EST  
**To:** "Carroll, Judy" (b)(6) "Feinberg, Mark"  
(b)(6)  
**Cc:** "Widdowson, Marc-Alain (CDC/OID/NCIRD)" <[zux5@cdc.gov](mailto:zux5@cdc.gov)>, "Messonnier, Nancy (CDC/OID/NCIRD)" <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Subject:** RE: arranging for a call

Hi Judy: Dr. Schuchat stated that this call can be an hour if needed, so they can stay on the call for a whole hour, however she may not be available for the entire call. Just FYI thanks.  
-Dawn

---

**From:** Carroll, Judy (b)(6)  
**Sent:** Tuesday, November 25, 2014 10:50 AM  
**To:** King, Dawn R. (CDC/OID/NCIRD) (CTR)  
**Subject:** RE: arranging for a call

Hi Dawn ...

I called, but got your voicemail. This call is the priority and we will reschedule the conflict. I will send a meeting request with call in details for Monday at 11:00 am.

Thanks,  
Judy

---

**From:** King, Dawn R. (CDC/OID/NCIRD) (CTR) [<mailto:duk3@cdc.gov>]  
**Sent:** Tuesday, November 25, 2014 10:25 AM  
**To:** Carroll, Judy  
**Subject:** RE: arranging for a call

Please call me: 404-639-1540. As I was so happy we could do 11:00 collectively.

---

**From:** Carroll, Judy (b)(6)  
**Sent:** Tuesday, November 25, 2014 10:23 AM  
**To:** King, Dawn R. (CDC/OID/NCIRD) (CTR)  
**Subject:** RE: arranging for a call

Hi Dawn ...

Mark now has a conflict on Monday at 11:00 am. Is 1:00 pm possible for Dr. Schuchat, Marc-Alain and Nancy?

Thanks,  
Judy

---

**From:** Carroll, Judy  
**Sent:** Tuesday, November 25, 2014 8:43 AM  
**To:** 'King, Dawn R. (CDC/OID/NCIRD) (CTR)'  
**Subject:** RE: arranging for a call

Hi Dawn,

Yes, December 1<sup>st</sup>. (b)(6)  
If Monday is not possible for Dr. Schuchat, can you let me know if something is possible on Wednesday, December 3?

Thanks,  
Judy

---

**From:** King, Dawn R. (CDC/OID/NCIRD) (CTR) [<mailto:duk3@cdc.gov>]  
**Sent:** Tuesday, November 25, 2014 8:37 AM  
**To:** Carroll, Judy  
**Subject:** RE: arranging for a call



Hi Judy:

Is that Monday December 1<sup>st</sup>? also, are they available at all on Tuesday afternoon between 2:00 and 4:30? If Monday is the only time, I understand, but Dr. Schuchat may not be able to participate.

Thanks,

Dawn King



Contractor  
Executive Assistant to Dr. Anne Schuchat  
Director, National Center for Immunization and Respiratory Diseases  
Centers for Disease Control and Prevention  
1600 Clifton Road, N.E. Mailstop A-27  
Atlanta, GA 30333  
404-639-1540

---

**From:** Carroll, Judy (b)(6)  
**Sent:** Tuesday, November 25, 2014 8:13 AM  
**To:** King, Dawn R. (CDC/OID/NCIRD) (CTR)  
**Subject:** RE: arranging for a call

Dear Dawn,

Mark Feinberg, Jim Robinson and Sangeetha Sagar are available for a call on Monday, December 11:00 am – 12:00 pm or 1:00 – 1:30 pm. Can you please let me know if either time will work for those attending from the CDC?

Thank you,

Judy Carroll

(b)(6)

Assistant to:  
Marian Wentworth, VP Global Vaccines Strategy & Innovation  
Jim Adair, Exec. Director, Global Vaccines Strategy & Innovation  
Kishna Kalicharran, Exec. Director, Global External Alliances, Vaccines  
John Lanphear, Exec. Director, Customer Centricity & Customer Insights

**From:** Schuchat, Anne MD (CDC/OID/NCIRD) [<mailto:acs1@cdc.gov>]  
**Sent:** Monday, November 24, 2014 4:41 PM  
**To:** Feinberg, Mark; King, Dawn R. (CDC/OID/NCIRD) (CTR)  
**Cc:** Widdowson, Marc-Alain (CDC/OID/NCIRD); Messonnier, Nancy (CDC/OID/NCIRD); Sagar, Sangeetha L; Robinson, James; Keane, Maggie; Brown, Arlene F; Carroll, Judy  
**Subject:** RE: arranging for a call

Thanks Mark – Dawn King can assist w/ the scheduling from CDC, making sure Marc-Alain and Nancy are available, and working w/ Arlene and Judy to coordinate the schedules of your folks.

Anne Schuchat, MD  
RADM, US Public Health Service  
Assistant Surgeon General  
Director, National Center for Immunization and Respiratory Diseases  
Mailstop A-27  
Centers for Disease Control and Prevention  
Atlanta, GA 30333  
Phone: 404-639-8200

---

**From:** Feinberg, Mark (b)(6)  
**Sent:** Monday, November 24, 2014 4:21 PM  
**To:** Schuchat, Anne MD (CDC/OID/NCIRD)  
**Cc:** Widdowson, Marc-Alain (CDC/OID/NCIRD); Messonnier, Nancy (CDC/OID/NCIRD); Sagar, Sangeetha L; Robinson, James; Keane, Maggie; Brown, Arlene F; Carroll, Judy  
**Subject:** Re: arranging for a call

Dear Anne,

Thanks very much. We would be very happy to connect with you all to discuss these important issues. We can certainly try to find time early next week. On our end, Arlene Brown and Judy Carroll can help try to coordinate schedules. Is there someone at the CDC who they can work with?

Also, while you note below provides very helpful context, it would be helpful for us to know the range of specific questions you would like to have addressed. This will help us do our best to pull this information together as well as identify the range of people we will want to include on the call. At a minimum, hopefully my manufacturing (Jim Robinson) and Bioprocess (Sangeetha Sagar) colleagues will be able to participate.

We look forward to talking with you and hopefully having the opportunity to work with you to accelerate the evaluation and delivery of an effective and safe Ebola vaccine.

I hope you all can find at least a bit of free time to have a great Thanksgiving holiday.

Best,

Mark

Mark Feinberg, MD, PhD

(b)(6)

On Nov 24, 2014, at 4:02 PM, Schuchat, Anne MD (CDC/OID/NCIRD) <[acs1@cdc.gov](mailto:acs1@cdc.gov)> wrote:

Mark – I'm sure you are deluged with today's announcement, (b)(4)

(b)(4)

(b)(4) it would be helpful if our key folks (Drs. Widdowson, Messonnier and I) could arrange to have a call with you soon. In particular, it would be helpful to get a clearer sense of the timing for key phase I studies and their results, which would be needed for dose selection, and then the following time for preparation of appropriate formulations for use in the W Africa trial context. We are also incorporating information from a WHO assessment of the cold chain in country and working out what we need to establish for product handling and storage, so getting more insight from you on that would also be helpful. I think early next week would be good if you want to consider that – can work out more specifics probably w/ those on the cc line. Look forward to speaking with you soon.

Anne Schuchat, MD  
RADM, US Public Health Service  
Assistant Surgeon General  
Director, National Center for Immunization and Respiratory Diseases  
Mailstop A-27  
Centers for Disease Control and Prevention  
Atlanta, GA 30333  
Phone: 404-639-8200

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (One Merck Drive, Whitehouse Station, New Jersey, USA 08889), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (One Merck Drive, Whitehouse Station, New Jersey, USA 08889), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential,



proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (One Merck Drive, Whitehouse Station, New Jersey, USA 08889), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (One Merck Drive, Whitehouse Station, New Jersey, USA 08889), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (One Merck Drive, Whitehouse Station, New Jersey, USA 08889), and/or its affiliates Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Kuter, Barbara J.  
**Sent:** Wed, 1 Jan 2020 22:41:09 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** (b)(6)  
**Subject:** Update

Nancy,

Happy New Year!

I wanted to let you know that (b)(6) will be my last day at Merck. It has been a great honor to work on many pediatric and adolescent vaccines during my time at Merck and to work with experts such as you.

I plan to continue to remain active in the vaccine field and would love to continue to collaborate whenever possible.

Please update your contact information for me as follows:

Email: (b)(6)  
Cell: (b)(6)  
Home: (b)(6)

All the best in the New Year and I hope to see you again soon!

Barb

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Ritchey, Julian /US  
**Sent:** Thu, 2 Jan 2020 17:32:40 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** Automatic reply: Influenza EO outreach

Thank you for your message.  
I am out of the office with limited access to email.  
I'll be in touch upon my return in the next decade!  
Enjoy your holidays.

**From:** Villar, Carmen Sachiko  
**Sent:** Wed, 22 Jan 2020 20:02:54 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** Butler, Jay C. (CDC/DDID/OD); Aleshire, Noah (CDC/DDID/NCIRD/OD); Mbaeyi, Sarah A. (Meyer) (CDC/DDID/NCIRD/DBD)  
**Subject:** RE: vaccine confidence

Hi Nancy and thanks for the quick reply. No worries on timing. I completely understand. The news on the coronavirus sounds scary. Anything we can do to help, just let us know.

Noah and Sarah – We will be in touch soon to schedule a call.

Best to all of my CDC family.  
Carmen

---

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Sent:** Wednesday, January 22, 2020 2:23 PM  
**To:** Villar, Carmen Sachiko <(b)(6)>  
**Cc:** Butler, Jay C. (CDC/DDID/OD) <jcb3@cdc.gov>; Aleshire, Noah (CDC/DDID/NCIRD/OD) <uwo2@cdc.gov>; Mbaeyi, Sarah A. (Meyer) (CDC/DDID/NCIRD/DBD) <vif6@cdc.gov>  
**Subject:** RE: vaccine confidence

**EXTERNAL EMAIL** – Use caution with any links or file attachments.

Thanks Carmen. We are very excited to hear what you have been working on. Noah and Sarah (cc'ed here) are coordinating much of these efforts. Suggest we schedule some time to talk? As you can imagine, we are very buried in this coronavirus outbreak so I might suggest that we wait a few weeks for a meeting?

Thanks,  
Nancy

---

**From:** Villar, Carmen Sachiko <(b)(6)>  
**Sent:** Wednesday, January 22, 2020 1:54 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>; Butler, Jay C. (CDC/DDID/OD) <jcb3@cdc.gov>  
**Subject:** FW: vaccine confidence

Hi Nancy and Jay!

I didn't really get to catch up with you guys on the call between Merck and CDC, but I did want to follow up on the vaccine confidence issue and Amanda recommended I reach out to you. The policy team in our vaccine unit here has been doing a lot of work this past year on vaccine confidence. I know they would be happy to connect with the appropriate CDC folks to see how we might be able to support efforts around this critical PH issue. If you could let me know the best person to put in touch with my folks, I would greatly appreciate it.  
Hope all is well in Atlanta!



Best,  
Carmen

---

**From:** Campbell, Amanda (CDC/OD/OCS) <[ons3@cdc.gov](mailto:ons3@cdc.gov)>  
**Sent:** Wednesday, January 22, 2020 1:39 PM  
**To:** Villar, Carmen Sachiko (b)(6)  
**Subject:** RE: vaccine confidence

**EXTERNAL EMAIL** – Use caution with any links or file attachments.  
Hi Carmen,

I'd recommend reaching to both Nancy and Jay.

Thanks!  
Amanda

Amanda Campbell  
*Deputy Chief of Staff*  
*Office of the Director*  
*Centers for Disease Control and Prevention*  
1600 Clifton Rd NE  
Atlanta, GA 30329  
470-316-2028  
[ons3@cdc.gov](mailto:ons3@cdc.gov)

---

**From:** Villar, Carmen Sachiko (b)(6)  
**Sent:** Wednesday, January 22, 2020 1:09 PM  
**To:** Campbell, Amanda (CDC/OD/OCS) <[ons3@cdc.gov](mailto:ons3@cdc.gov)>  
**Subject:** vaccine confidence

Hi Amanda,  
I mentioned the interest in vaccine confidence to my policy colleagues over in vaccines. They would love to discuss further. I just wasn't sure who to connect them to and thought I would ask you what Dr Redfield would prefer. I could reach out to Nancy M for the connection or Jay B. Just let me know what you'd advise.  
Thanks!  
Carmen

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error,

please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Ritchey, Julian /US  
**Sent:** Thu, 30 Apr 2020 14:44:51 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** checking in

Yes – that would be most helpful.

At your convenience.

My cell: (b)(6)

**From:** "nar5@cdc.gov" <nar5@cdc.gov>

**Date:** Thursday, April 30, 2020 at 10:38 AM

**To:** "Ritchey, Julian /US" <(b)(6)>

**Subject:** [EXTERNAL] checking in

**EXTERNAL :** Real sender is nar5@cdc.gov

Do we need to check in before today's call?

**From:** Jansen, Kathrin  
**Sent:** Tue, 5 May 2020 18:19:22 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** RE: chat

Great looking forward to it

---

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Sent:** Tuesday, May 5, 2020 2:16 PM  
**To:** Jansen, Kathrin <(b)(6)>  
**Subject:** [EXTERNAL] RE: chat

Yes, I can make that work. Just have to be done by 4. I'll call you.

---

**From:** Jansen, Kathrin <(b)(6)>  
**Sent:** Tuesday, May 5, 2020 1:53 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Subject:** RE: chat

That would be great Nancy; how does 3:30 pm today sound, I have 45 minutes before going into another call at 4:15pm. Alternatively later today. My cell phone is (b)(6) Best Kathrin

---

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Sent:** Tuesday, May 5, 2020 1:33 PM  
**To:** Jansen, Kathrin <(b)(6)>  
**Subject:** [EXTERNAL] chat

Let me know if you have a few minutes to talk about COVID vaccines.  
Nancy



**From:** Jansen, Kathrin  
**Sent:** Sun, 10 May 2020 18:13:51 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Santos, Michael (FNIH) [T]; Lowy, Douglas (NIH/NCI) [E]  
**Cc:** Schrag, Stephanie (CDC/DDID/NCIRD/DBD); Verani, Jennifer R. (CDC/DDID/NCIRD/DBD); Thornburg, Natalie (CDC/DDID/NCIRD/DVD); Erbeling, Emily (NIH/NIAID) [E]  
**Subject:** RE: Review requested: Human Challenge Model draft; notes from Vaccines Sub-Groups, ACTIV Leadership Team, and Preclinical WG

Thank you Nancy for your support and yes it would be great to have Stephanie, Natalie and Jennifer joining. Mike can provide you with all the communications as he has it all at his fingertips, no doubt. Best regards Kathrin

---

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Sent:** Sunday, May 10, 2020 1:14 PM  
**To:** Santos, Michael (FNIH) [T] <msantos@fnih.org>; Jansen, Kathrin <(b)(6)>  
**Cc:** Schrag, Stephanie (CDC/DDID/NCIRD/DBD) <zha6@cdc.gov>; Verani, Jennifer R. (CDC/DDID/NCIRD/DBD) <qzr7@cdc.gov>; Thornburg, Natalie (CDC/DDID/NCIRD/DVD) <nax3@cdc.gov>; Erbeling, Emily (NIH/NIAID) [E] <emily.erbeling@nih.gov>  
**Subject:** [EXTERNAL] RE: Review requested: Human Challenge Model draft; notes from Vaccines Sub-Groups, ACTIV Leadership Team, and Preclinical WG

Michael and Kathrin

To ensure that CDC can provide the level of input which is being requested, please add Stephanie Schrag and Jennifer Verani, who are leading CDC coronavirus vaccine evaluation activities, and Natalie Thornburg, who leads COVID serology activities, to the overall ACTIV group. I think that Stephanie and Jennifer would be helpful additions to the subgroup considering the design of a phase III study. Kathrin has been asking for information about ongoing natural history and serology studies and Natalie would be well placed to discuss CDC's work.

I can send them some of the notes from the previous meetings so they can get caught up but I was wondering if you have that posted somewhere that they could access, if that's easier.

Thank you,  
Nancy

---

**From:** Santos, Michael (FNIH) [T] <msantos@fnih.org>  
**Sent:** Saturday, May 9, 2020 10:16 PM  
**To:** <(b)(6)> Lowy, Douglas (NIH/NCI) [E] <LowyD@mail.nih.gov>; <(b)(6)> Arvin, Ann <aarvin@stanford.edu>; Beth Bell <(b)(6)> <(b)(6)>; <(b)(6)> susan.buchbinder@sfdph.org; lcorey@fredhutch.org; mmdavis@stanford.edu; Emilio.Emini@gatesfoundation.org; <(b)(6)> Haynes, Barton <hayne002@mc.duke.edu>; hotez@bcm.edu; lanzavecchia@irb.usi.ch; Marks, Peter (FDA/CBER) <Peter.Marks@fda.hhs.gov>; Mascola, John (NIH/VRC) [E] <jmascola@mail.nih.gov>; Messonnier, Nancy



(CDC/DDID/NCIRD/OD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>; Michael, Nelson L CIV USARMY MEDCOM WRAIR (USA) <[nelson.l.michael2.civ@mail.mil](mailto:nelson.l.michael2.civ@mail.mil)>; Offit, Paul <[offit@email.chop.edu](mailto:offit@email.chop.edu)>; [HSchuite@its.jnj.com](mailto:HSchuite@its.jnj.com); Seals, Jonathan (OS/ASPR/BARDA) <[jonathan.seals@hhs.gov](mailto:jonathan.seals@hhs.gov)>; (b)(6) Tal Zaks

(b)(6)  
Cc: Tolman, Brett (b)(6); Austin, Sarah (NIH/NIAID) [E] <[austinsj@niaid.nih.gov](mailto:austinsj@niaid.nih.gov)>; (b)(6) Shannon.Devine@duke.edu; (b)(6) Johnson, Maureen (NIH/NCI) [E] <[johnsonr@dea.nci.nih.gov](mailto:johnsonr@dea.nci.nih.gov)>; Kozlowski, Mary (NIH/NCI) [C] <[mary.kozlowski@nih.gov](mailto:mary.kozlowski@nih.gov)>; [bminnich@fredhutch.org](mailto:bminnich@fredhutch.org); (b)(6) kelly.soderberg@duke.edu; Douglas.SorianoOsejo@bcm.edu; Suhana, Tina (NIH/VRC) [E] <[esuhana@mail.nih.gov](mailto:esuhana@mail.nih.gov)>; (b)(6); Cohen, Myron <[myron\\_cohen@med.unc.edu](mailto:myron_cohen@med.unc.edu)>; Douoguih, Macaya [JRDUS] <[MDouogui@its.jnj.com](mailto:MDouogui@its.jnj.com)>; Erbelding, Emily (NIH/NIAID) [E] <[emily.erbelding@nih.gov](mailto:emily.erbelding@nih.gov)>; Gilbert PhD, Peter B <[pgilbert@scharp.org](mailto:pgilbert@scharp.org)>; Paul Gillard (b)(6) Gruber, Marion (FDA/CBER) <[Marion.Gruber@fda.hhs.gov](mailto:Marion.Gruber@fda.hhs.gov)>; Gurunathan, Sanjay /US (b)(6); Hamilton, Holli (OS/ASPR/BARDA) <[Holli.Hamilton@hhs.gov](mailto:Holli.Hamilton@hhs.gov)>; (b)(6) Ledgerwood, Julie (NIH/NIAID) [E] <[JUMARTIN@niaid.nih.gov](mailto:JUMARTIN@niaid.nih.gov)>; Leyssen, Maarten [JRDNL] <[MLeyssen@its.jnj.com](mailto:MLeyssen@its.jnj.com)>; Marovich, Mary (NIH/NIAID) [E] <[mary.marovich@nih.gov](mailto:mary.marovich@nih.gov)>; Kathleen Neuzil <[kneuzil@som.umaryland.edu](mailto:kneuzil@som.umaryland.edu)>; Robb, Merlin <[mrobb@hivresearch.org](mailto:mrobb@hivresearch.org)>; [Sahin@Uni-Mainz.de](mailto:Sahin@Uni-Mainz.de); Michael Watson (x) <(b)(6)>; Parker, Ashley (NIH/OD) [E] <[ashley.parker@nih.gov](mailto:ashley.parker@nih.gov)>; Qashu, Felicia (NIH/OD) [E] <[felicia.qashu@nih.gov](mailto:felicia.qashu@nih.gov)>; Colvis, Christine (NIH/NCATS) [E] <[Christine.Colvis@nih.gov](mailto:Christine.Colvis@nih.gov)>; (b)(6) (b)(6); Kurilla, Michael (NIH/NCATS) [E] <[michael.kurilla@nih.gov](mailto:michael.kurilla@nih.gov)>; Read, Sarah (NIH/NIAID) [E] <[reads@niaid.nih.gov](mailto:reads@niaid.nih.gov)>; [john.young.jy3@roche.com](mailto:john.young.jy3@roche.com); Menetski, Joseph (FNIH) [T] <[jmenetski@fnihi.org](mailto:jmenetski@fnihi.org)>; Alvarez, Rosa Maria (b)(6); Adam, Stacey (FNIH) [T] <[sadam@fnihi.org](mailto:sadam@fnihi.org)>; Kim, Elizabeth (b)(6) Tountas, Karen (FNIH) [T] <[ktountas@fnihi.org](mailto:ktountas@fnihi.org)>; Wachtel, Jonathan (b)(6); Wholley, David (FNIH) [T] <[dwholley@fnihi.org](mailto:dwholley@fnihi.org)>; Gonzalez, Nina (b)(6) Stratton, Benjamin (b)(6)

**Subject:** Review requested: Human Challenge Model draft; notes from Vaccines Sub-Groups, ACTIV Leadership Team, and Preclinical WG

Dear Vaccines Working Group members (and cc'ing others for awareness),

This note is an omnibus update for the Working Group: Sub-Group meeting notes, the human challenge model draft and agenda for the Working Group meeting, upcoming Vaccines Clinical Trial Sub-Group meetings and topics, and for awareness notes from the ACTIV Leadership Team meeting and Preclinical WG.

#### Sub-Group meeting notes

As a reminder, the Protective Immune Responses and Vaccine-associated Immune Enhancement Sub-Groups met since our last Working Group meeting (Thurs and Fri, respectively). Thank you to all who participated or sent input. **Attached are the notes and action items from each meeting.** The agendas and meeting materials and pre-reads are embedded in those documents. If anyone would like to be added to the lists for either Sub-Group, please let us know.

**Review Controlled Human Infection Model outline** in preparation for Monday's Working Group meeting

The main agenda item at the next Vaccines Working Group meeting, Monday, 12pm ET (9am PT / 6pm CEST), is a discussion of the Working Group's perspective on a CoV-2 controlled human infection model. Please review the attached outline to prepare for that discussion. If you cannot attend the meeting, feel free to send input via email that we can represent.

#### Vaccines Clinical Trial Sub-Group updates

Members of this Sub-Group are invited on Tuesday (11am ET) to join the Clinical Trial Capacity Working Group meeting, where Paula and Larry will share the plans of the Sub-Group and the CTC WG will share their activities and how they can work with us (e.g., inventory trial site capacity). **The Sub-Group meeting Wednesday (1pm ET) will focus on key protocol questions.**

#### ACTIV Leadership Team meeting notes

Last Wednesday, the ACTIV Leadership Team (the parent body above the Working Groups) met. Kathrin and Doug presented the progress and plans of the Working Group and answered questions. The meeting presentation and notes are attached. **Note: This is a good way to see a high-level summary of the activities of the other Working Groups, many of which are relevant to our work;** if you have specific questions, let us know and we can follow up.

#### Pre-clinical Working Group

Finally, as discussed last week we will continue to share notes from the Preclinical Working Group for awareness (attached zip file). **Note: a request to review the data collection fields for animal models will be coming to our group,** which we will circulate to the Protective Immune Responses and Vaccine-associated Immune Enhancement Sub-Groups.

As always, please don't hesitate to reach out with any questions or suggestions.

Best regards,  
Brett and Mike

**Michael Santos, PhD**

Associate Vice President, Science

**Foundation for the National Institutes of Health**

301-402-6917 | [fnihi.org](https://fnihi.org)

11400 Rockville Pike, Suite 600, North Bethesda, MD 20852



Stay at the forefront of FNIH news: [fnihi.org/newsletter](https://fnihi.org/newsletter)



**From:** Jansen, Kathrin  
**Sent:** Tue, 26 May 2020 10:26:21 +0000  
**To:** Verani, Jennifer R. (CDC/DDID/NCIRD/DBD); Santos, Michael (FNIH) [T]; Messonnier, Nancy (CDC/DDID/NCIRD/OD); Tolman, Brett; Lowy, Douglas (NIH/NCI) [E]  
**Cc:** Schrag, Stephanie (CDC/DDID/NCIRD/DBD); Biggerstaff, Matthew (CDC/DDID/NCIRD/ID)  
**Subject:** RE: ACTIV vaccine working group meeting

Thank you Nancy and Jennifer, much appreciated. Best regards Kathrin

---

**From:** Verani, Jennifer R. (CDC/DDID/NCIRD/DBD) <qzr7@cdc.gov>  
**Sent:** Saturday, May 23, 2020 3:40 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>; Jansen, Kathrin <(b)(6)>  
**Cc:** Schrag, Stephanie (CDC/DDID/NCIRD/DBD) <zha6@cdc.gov>; Biggerstaff, Matthew (CDC/DDID/NCIRD/ID) <zmo2@cdc.gov>  
**Subject:** [EXTERNAL] RE: ACTIV vaccine working group meeting

Kathrin,

Matt Biggerstaff (cc'd here) from the CDC modeling team has kindly offered to present at vaccine working group meeting this Thursday (May 28). Should he plan to present at the start of the meeting (2pm?)

Regards,  
Jennifer

---

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Sent:** Saturday, May 23, 2020 2:08 PM  
**To:** Jansen, Kathrin <(b)(6)>  
**Cc:** Schrag, Stephanie (CDC/DDID/NCIRD/DBD) <zha6@cdc.gov>; Verani, Jennifer R. (CDC/DDID/NCIRD/DBD) <qzr7@cdc.gov>  
**Subject:** RE: ACTIV vaccine working group meeting

We'd be happy to. Jennifer and Stephanie can help coordinate with the modelers.

---

**From:** Jansen, Kathrin <(b)(6)>  
**Sent:** Saturday, May 23, 2020 10:05 AM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Subject:** ACTIV vaccine working group meeting

Dear Nancy, as briefly discussed by phone, <(b)(4)>

<(b)(4)>

(b)(4)

Thank you for your help and I hope you can enjoy the holiday weekend. Stay well, best Kathrin

**From:** Cane, Alejandro  
**Sent:** Thu, 11 Jun 2020 13:47:43 +0000  
**To:** Fox, Kimberley (CDC/DDID/NCIRD/DBD);Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** Wharton, Melinda (CDC/DDID/NCIRD/ISD)  
**Subject:** RE: Contact from Pfizer

Dear Kim,

Thank you very much for your contact.

I think, if you are available, we can prepare a meeting for June 23<sup>rd</sup> at 3 pm , in order to avoid any potential conflict with the scheduled ACIP virtual meeting on June 24<sup>th</sup>.

Please let me know if you want me sending an appointment and, if this is the case, who from your team I should include as well as you and Melinda.

From the Pfizer side, the participants will be me, Vinnie Snow ( as you know she is part of my team), David Hering (North America Vaccines Regional President) and Lisa Cohen ( Vaccines Corporate Affairs)

Looking forward to talk with you

Best regards,

Ale

---

**From:** Fox, Kimberley (CDC/DDID/NCIRD/DBD) <kaf6@cdc.gov>  
**Sent:** Wednesday, June 10, 2020 9:15 PM  
**To:** Cane, Alejandro <(b)(6)> Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Cc:** Wharton, Melinda (CDC/DDID/NCIRD/ISD) <mew2@cdc.gov>  
**Subject:** [EXTERNAL] RE: Contact from Pfizer

Dear Ale,

I will follow up for the scheduling. Would late afternoon (between 3 and 5 PM) on either June 23 or June 24 work for you? If not, I will look for times later that same week.

I look forward to talking with you.

Regards,

Kim

Kimberley Fox, MD, MPH  
Captain, USPHS  
Acting Director, Division of Bacterial Diseases  
National Center for Immunization and Respiratory Diseases  
Centers for Disease Control and Prevention  
Atlanta, GA USA

Tel 404-718-1408  
Cell 404-630-7555

---

**From:** Cane, Alejandro <(b)(6)>  
**Sent:** Wednesday, June 10, 2020 5:58 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Cc:** Fox, Kimberley (CDC/DDID/NCIRD/DBD) <[kaf6@cdc.gov](mailto:kaf6@cdc.gov)>; Wharton, Melinda (CDC/DDID/NCIRD/ISD) <[mew2@cdc.gov](mailto:mew2@cdc.gov)>  
**Subject:** RE: Contact from Pfizer

Dear Nancy,

Thank you very much! It is not even easy to imagine how busy you are. I really appreciate the time you've taken in your reply.

Kim and Melinda, it would be a pleasure to have a meeting ( at least virtually) with you and your teams as Nancy has suggested. Please let me know who from your teams can help me with the organization of the call.

I also wanted to reinforce the fact that personally, but also for the entire Pfizer Vaccines team is critical to continue building a strong relationship as well as to maintain a very open and transparent channel of communication with you.

Looking forward to meet you soon

Best regards,

Ale

Alejandro Cané, MD PhD  
North America Vaccines Medical and Scientific Affairs Lead  
Pfizer Biopharmaceuticals Group  
Complejo Thames Office Park  
Colectora Panamericana 1804, 1 Piso Sector "B" Lado Sur  
Villa Adelina (CP 1607EEV) Pcia Buenos Aires-Argentina  
Tel: (b)(6)  
Mobile: (b)(6)  
e mail: (b)(6)



---

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Sent:** Wednesday, June 10, 2020 6:07 PM  
**To:** Cane, Alejandro <(b)(6)>



**Cc:** Fox, Kimberley (CDC/DDID/NCIRD/DBD) <[kaf6@cdc.gov](mailto:kaf6@cdc.gov)>; Wharton, Melinda (CDC/DDID/NCIRD/ISD) <[mew2@cdc.gov](mailto:mew2@cdc.gov)>

**Subject:** [EXTERNAL] RE: Contact from Pfizer

My apologies. As you can imagine, it is an unimaginably busy time here. I think the best next step would be for your team to talk to the combination of Kim Fox, who took over for Barb Mahon, and Melinda Wharton, who directs ISD. Kim's group at DBD is the group that writes the recommendations but then Melinda's group is translating it into CDSi. We worked so hard to build on the relationship between CDC and Pfizer and I definitely want to continue to build on that.

Nancy

**From:** Cane, Alejandro (b)(6)  
**Sent:** Tuesday, June 9, 2020 3:39 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>  
**Subject:** FW: Contact from Pfizer

Dear Nancy,

I hope you and your family are remaining safe and well

I'm so sorry to bothering you again. I can't imagine how busy you are, and my intention is just to confirm you have received my previous contact.

I know these are not perfect times to ask for any kind of meeting but I was hoping you might have a few minutes to spare to speak on the topics listed in the email below

Thanks in advance for your time.

Best regards,

Ale

Alejandro Cané, MD PhD  
North America Vaccines Medical and Scientific Affairs Lead  
Pfizer Biopharmaceuticals Group  
Complejo Thames Office Park  
Colectora Panamericana 1804, 1 Piso Sector "B" Lado Sur  
Villa Adelina (CP 1607EEV) Pcia Buenos Aires-Argentina  
Tel: (b)(6)  
Mobile: (b)(6)  
e mail: (b)(6)



---

**From:** Cane, Alejandro

**Sent:** Friday, May 29, 2020 6:22 PM

**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>

**Cc:** Hering, David <(b)(6)>; Snow, Vincenza T <(b)(6)>

Coen, Lisa <(b)(6)>; Jodar, Luis <(b)(6)>; Fox, Kimberley

(CDC/DDID/NCIRD/DBD) <[kaf6@cdc.gov](mailto:kaf6@cdc.gov)>; MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)

<[aji8@cdc.gov](mailto:aji8@cdc.gov)>

**Subject:** Contact from Pfizer

Dear Nancy,

I hope you and your family are all doing well.

Many thanks to you and your staff for your hard work and dedication to public health during these difficulty times. As was agreed at the meeting we had in person on February 3, we have been working closely with Jessica MacNeil and Noah Aleshire to update ACIP on our pipeline and approved vaccines. We are very grateful for their time and assistance in getting us in touch with all the relevant work groups.

(b)(4)

I know how incredibly busy you are but I was hoping you, Melinda Wharton, and Jessica might have a few minutes to spare to speak with us on these topics?

Thanks in advance for your time.

Best regards,

Ale



Alejandro Cané, MD PhD  
North America Vaccines Medical and Scientific Affairs Lead  
Pfizer Biopharmaceuticals Group  
Complejo Thames Office Park  
Colectora Panamericana 1804, 1 Piso Sector "B" Lado Sur  
Villa Adelina (CP 1607EEV) Pcia Buenos Aires-Argentina

Tel: (b)(6)

Mobile: (b)(6)

e mail: (b)(6)



**Pfizer**  
Biopharmaceuticals  
Group

**From:** Ritchey, Julian /US  
**Sent:** Wed, 24 Jun 2020 02:30:01 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** RE: Routine Immunization Status by Age

Please do.

I'm happy to discuss any questions with them, answer (or get answers) to source data questions, etc.

We'd love to compare observations on the data.

And yes, it needs to be for your internal use only per our IQVIA contract.

Julian

---

**From:** "nar5@cdc.gov" <nar5@cdc.gov>  
**Date:** Tuesday, June 23, 2020 at 5:41 PM  
**To:** "Ritchey, Julian /US" (b)(6)  
**Subject:** [EXTERNAL] RE: Routine Immunization Status by Age

**EXTERNAL :** Real sender is nar5@cdc.gov

We have been trying to get more granular data, just like this. If its okay, I will share with Melinda, Jeanne, and Ram? Clearly for internal use only.  
And thanks.

---

**From:** Ritchey, Julian /US (b)(6)  
**Sent:** Tuesday, June 23, 2020 5:26 PM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Subject:** Routine Immunization Status by Age

Dear Nancy –

Thank you for your time on the call today with the STOP Coalition.

I appreciate your continuing to share updates in various forums on how your teams are approaching the season. It's good to hear that the discussion on timing seems to have settled on keeping the Press Conference on 10/1. And I took from the call you feel as I do the quantity of doses (between new and in market) is sufficient to support significantly raising rates.

On the topic of routine immunization, I thought you might be interested in the attached. (b)(4)

(b)(4)

(b)(4)

I suspect this is more in Melinda's and Jeanne's courts, but after today's discussion, I thought I'd share with you first as I think this will be an important issue to identify and monitor going forward to ensure progress against it. We'd be happy to discuss this and provide this to your team each month if this is information you don't already have and/or a projection that helps visualize the data more clearly. I'd welcome any thoughts you have on this.

Good luck with ACIP tomorrow. The team has been doing a great job amid the practical challenges to assemble a strong program.

Julian

**From:** Ritchey, Julian /US  
**Sent:** Tue, 23 Jun 2020 21:26:06 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** Routine Immunization Status by Age  
**Attachments:** State Claims\_External Parties v2[1].pptx

Dear Nancy –

Thank you for your time on the call today with the STOP Coalition.

I appreciate your continuing to share updates in various forums on how your teams are approaching the season. It's good to hear that the discussion on timing seems to have settled on keeping the Press Conference on 10/1. And I took from the call you feel as I do the quantity of doses (between new and in market) is sufficient to support significantly raising rates.

On the topic of routine immunization, I thought you might be interested in the attached. (b)(4)

(b)(4)

I suspect this is more in Melinda's and Jeanne's courts, but after today's discussion, I thought I'd share with you first as I think this will be an important issue to identify and monitor going forward to ensure progress against it. We'd be happy to discuss this and provide this to your team each month if this is information you don't already have and/or a projection that helps visualize the data more clearly. I'd welcome any thoughts you have on this.

Good luck with ACIP tomorrow. The team has been doing a great job amid the practical challenges to assemble a strong program.

Julian

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

**From:** Ritchey, Julian /US  
**Sent:** Thu, 13 Aug 2020 19:37:52 +0000  
**To:** Santoli, Jeanne (CDC/DDID/NCIRD/ISD);Messonnier, Nancy (CDC/DDID/NCIRD/OD);Wharton, Melinda (CDC/DDID/NCIRD/ISD)  
**Cc:** Binder, Tami /US  
**Subject:** Updated State Claims Data  
**Attachments:** State Claims\_External Parties 08062020.pptx

Dears --

Sharing revised claims data as previously discussed.

(b)(4)

Please let me know if this continues to be useful for you as well as any questions or suggestions. As always regarding this - and any messaging which we could amplify - we would be very interested in more granular conversations between our subject matter experts while there is still time to shape messaging, particularly flu.

I welcome your feedback and thoughts --  
Julian



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



**From:** Ritchey, Julian /US  
**Sent:** Fri, 14 Aug 2020 15:01:26 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** Automatic reply: Updated State Claims Data

Thank you for your message.  
I am out of the office on vacation with limited access to email.  
I'll be in touch upon my return.

**From:** Grabenstein, John D.  
**Sent:** Wed, 16 May 2018 20:26:53 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** RE: The Washington Post: The Cybersecurity 202: Why cybersecurity experts are so concerned about the health-care industry

She said she enjoyed both the lectures and the dinner immensely.

Ah, these civilians. Always confused about sergeants major and lieutenant commanders... 😊

John

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [mailto:nar5@cdc.gov]  
**Sent:** Wednesday, May 16, 2018 16:20  
**To:** Grabenstein, John D.  
**Subject:** RE: The Washington Post: The Cybersecurity 202: Why cybersecurity experts are so concerned about the health-care industry

**EXTERNAL EMAIL** – Use caution with any links or file attachments.

Hi. We missed you. I presume Kathleen told you that we met and enjoyed a lovely dinner together. She also did not have to use your tutorial about my rank since I retired as of December 1.

**From:** Grabenstein, John D. (b)(6)  
**Sent:** Wednesday, May 16, 2018 4:12 PM  
**To:** Wharton, Melinda (CDC/OID/NCIRD) <mew2@cdc.gov>; Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>; Cohn, Amanda (CDC/OID/NCIRD) <anc0@cdc.gov>  
**Subject:** FW: The Washington Post: The Cybersecurity 202: Why cybersecurity experts are so concerned about the health-care industry

Drs. Wharton, Messonnier, Cohn,

I'm sorry not to be able to join you personally in Atlanta this week.

In case your clipping services didn't bring this article from the *Washington Post* to your attention, I want to suggest it. Note the comment about perceived vulnerabilities in public-health IT security.

**"In a poll of more than 500 security professionals, 51 percent of them said the health-care and public-health sectors were the least prepared for cyberattacks.** The pros said the industry was the most vulnerable among the country's 16 critical infrastructure sectors — and 85 percent of them said a major cyberattack on critical infrastructure was likely in the next five years."

<https://www.washingtonpost.com/news/powerpost/paloma/the-cybersecurity-202/2018/05/16/the-cybersecurity-202-why-cybersecurity-experts-are-so-concerned-about-the-health-care-industry/5afb102130fb042588799518/>

My memories of the effects of the cyber-attack on Merck are deep and fresh.

Best regards, John

---

**From:** Grabenstein, John D.  
**Sent:** Wednesday, May 16, 2018 11:49  
**To:** Grabenstein, John D.  
**Subject:** The Washington Post: The Cybersecurity 202: Why cybersecurity experts are so concerned about the health-care industry

I thought you might like this story from The Washington Post.

The Cybersecurity 202: Why cybersecurity experts are so concerned about the health-care industry  
Research released by two security companies paints an unsettling picture.

<https://www.washingtonpost.com/news/powerpost/paloma/the-cybersecurity-202/2018/05/16/the-cybersecurity-202-why-cybersecurity-experts-are-so-concerned-about-the-health-care-industry/5afb102130fb042588799518/>

From mobile phone ...  
John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Vaccines

(b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error,

please notify us immediately by reply e-mail and then delete it from your system.

**From:** Grabenstein, John D.  
**Sent:** Thu, 24 May 2018 12:58:37 +0000  
**To:** 'Patrick, Elizabeth'; Monroe, Judith (CDC cdcfoundation.org); Messonnier, Nancy (CDC/OID/NCIRD); WDowdle@taskforce.org; Hinman, Alan (CDC taskforce.org); Taylor, Kathleen A  
**Cc:** Conner, Dion; Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: Jeryl Lynn Hilleman Endowed Lecture-May 15 Hilton Atlanta

I missed the event of the year.

So glad the audience had a great chance to learn and reflect!

John

**From:** Patrick, Elizabeth [mailto:epatrick@CDCFoundation.org]  
**Sent:** Wednesday, May 23, 2018 17:31  
**To:** Monroe, Judy; nar5@cdc.gov; WDowdle@taskforce.org; ahinman@taskforce.org; Taylor, Kathleen A  
**Cc:** Conner, Dion; wjn4@cdc.gov; Grabenstein, John D.  
**Subject:** RE: Jeryl Lynn Hilleman Endowed Lecture-May 15 Hilton Atlanta

**EXTERNAL EMAIL** – Use caution with any links or file attachments.

Dear All,

I wanted to take the opportunity to thank the Hilleman Selection Committee for selecting two wonderful (and timely) speakers in Dr. Tumpey and Mr. Barry for the 2018 Hilleman Lecture to speak on the 1918 Influenza Pandemic! I want to thank Dr. Monroe and Dr. Messonnier for speaking, as well as Kathleen Taylor for speaking on behalf of Dr. Grabenstein from Merck. We had 375 registrants and about 200 attendees, which was still a good number for a conference registration. We had a lovely dinner with the selection committee and lecturers following the lecture at Nikolai's Roof. We missed Dr. Dowdle and his wife Mabel, but we were also joined by Ellen Cameron from Merck, as well as Dr. Gary Noble.

I wanted to also share that the CDC Foundation is posting a Blog Post (and sharing on social media) on the Hilleman Lecture. Thank you again for all of your support of the CDC Foundation and the Hilleman Lecture!

BLOG LINK: <https://www.cdcfoundation.org/blog/hilleman-endowed-lectureship-focuses-1918-influenza-pandemic>

FB LINK:

<https://www.facebook.com/CDCFoundation/photos/a.10150284475293053.331902.56439113052/10155419689918053/?type=3&theater>





Thank you,

**Elizabeth Patrick**

Donor Relations Officer

404-523-1873

[epatrick@cdcfoundation.org](mailto:epatrick@cdcfoundation.org)

[www.cdcfoundation.org](http://www.cdcfoundation.org)

[twitter](#) . [linkedin](#) . [facebook](#) . [instagram](#)



**From:** Patrick, Elizabeth

**Sent:** Thursday, April 26, 2018 4:25 PM

**To:** Monroe, Judy <[jmonroe@cdcfoundation.org](mailto:jmonroe@cdcfoundation.org)>; [nar5@cdc.gov](mailto:nar5@cdc.gov); [WDowdle@taskforce.org](mailto:WDowdle@taskforce.org); [ahinman@taskforce.org](mailto:ahinman@taskforce.org); (b)(6)

**Cc:** Conner, Dion <[dconner@cdcfoundation.org](mailto:dconner@cdcfoundation.org)>; [wjn4@cdc.gov](mailto:wjn4@cdc.gov); (b)(6)

**Subject:** Jeryl Lynn Hilleman Endowed Lecture-May 15 Hilton Atlanta

Dear All,

I hope everyone is doing well, and having a nice week! I wanted to send you an update regarding the [Jeryl Lynn Hilleman/ Merck Company Foundation Endowed Lectureship](#), which will take place at the [48<sup>th</sup> National Immunization Conference](#) at the [Hilton Atlanta, 255 Courtland Street, NE, Atlanta, GA](#) on **Tuesday, May 15, 5:30-7:00 p.m., in the Grand Ballroom on the 2<sup>nd</sup> floor**, with dinner to follow at Nikolai's Roof (in the Hilton (same building) on the 30<sup>th</sup> floor).

We are looking forward to hearing from our two speakers on the **1918 Influenza Pandemic**, **Dr. Terry Tumpey, Chief of the Immunology and Pathogenesis Branch of the CDC's Influenza Division Centers for Disease Control and Prevention (CDC)** and **Mr. John M. Barry, Author of *The Great Influenza***. Dr. John Grabenstein from Merck is unable to join us due to a scheduling conflict, but we will have Kathleen A. Taylor, Director, Global Healthcare Medical Affairs, Merck (copied here) speaking in his stead and joining us for dinner. Other dinner guests will include: Ellen Cameron, Associate Director, US Advocacy and Professional Affairs at Merck and Alison Thompson, Associate Vice President for Advancement at the CDC Foundation, as well as Dr. Walt Dowdle's lovely wife, Mrs. Mabel Dowdle.

The selection committee and speakers will gather after the lecture by the door of the Grand Ballroom and go up to Nikolai's Roof together, and **our dinner reservation is for 7:15 p.m.**

I am attaching our "Run of Show" for the evening, and please let me know if you have any questions. I look forward to seeing you all soon!

Thank you,

**Elizabeth Patrick**

Donor Relations Officer

404-523-1873

[epatrick@cdcfoundation.org](mailto:epatrick@cdcfoundation.org)

[www.cdcfoundation.org](http://www.cdcfoundation.org)

[twitter](#) . [linkedin](#) . [facebook](#) . [instagram](#)



Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error,



please notify us immediately by reply e-mail and then delete it from your system.

**From:** Grabenstein, John D.  
**Sent:** Thu, 28 Jun 2018 21:26:04 +0000  
**To:** Cohn, Amanda (CDC/OID/NCIRD); Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Yoder, Gregory A; Khan, Amir; Annunziato, Paula W.; Barr, Eliav  
**Subject:** RE: Updating CDC on Merck vaccine pipeline

CAPT Cohn, Dr. Rosenstein,

As we discussed last year about this time, Merck scientists would like to return to CDC in Atlanta to present your relevant subject matter experts an update on our vaccine pipeline. We suggest a mutually convenient date in November. We would like to offer the information to you under a confidential disclosure agreement.

As we develop an agenda, (b)(4)  
(b)(4)  
(b)(4) Further, we would like to discuss expanded cohorts or indications for HPV vaccination. Our pneumococcal team and your pneumococcal team intend to have a separate all-day session on a different date, perhaps in October.

We would appreciate if you could update us on your surveillance plans for RSV and CMV and other relevant scientific developments on your side.

We can update each other on work with global health stakeholders.

We are open to all your suggestions.

Best regards, John

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Research Laboratories  
351 N. Sumneytown Pike, UG-2B09  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk (b)(6)

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Research Laboratories  
351 N. Sumneytown Pike, UG-2B09  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk

(b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** (b)(6)  
**Sent:** Wed, 11 Jul 2018 00:16:57 +0000  
**To:** (b)(6) baltimo@caltech.edu; Messonnier, Nancy (CDC/OID/NCIRD) (b)(6)  
**Cc:** (b)(6) catharine.paules@nih.gov; Conrad, Patricia (NIH/NIAID) [E]; Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Session Accepted  
**Attachments:** [EXTERNAL] AAAS 2019 Annual Meeting Proposal Decision (Session ID #21433), AAAS Flu Vaccine Proposal-Submission.pdf

Dear Gary, David, Nancy and Anthony,

I am excited to share that our Universal Flu session proposal was accepted by the AAAS review committee!

Attached is the email I received today -- and a copy of our submission.

As a first step, AAAS is asking if you have any scheduling restrictions from Friday, Feb 15 through Sun, Feb 17, 2019. If you would **send me any conflicts by July 23<sup>rd</sup>**, then I'll consolidate and follow-up with the coordinators.

AAAS will reach out to you directly on Aug 1<sup>st</sup> -- to confirm your participation, review your presentation title and complete some paperwork -- if you can keep an eye out for that email.

Looking forward to the opportunity to work together to create an impactful session!

Best,  
Karen

Karen CHANDROSS, PhD

Strategic Initiatives & Scientific Relations  
Program Director, iDEA awards

Sanofi R&D

TE (b)(6) CELL: (b)(6) (b)(6)

**From:** Chandross, Karen /US  
**Sent:** Thursday, April 19, 2018 1:53 PM  
**To:** 'Baltimore, David' <baltimo@caltech.edu>; 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; (b)(6) Nabel, Gary /US (b)(6)  
**Cc:** Wei, Ronnie /US (b)(6) Travayiakis, Carol /US (b)(6); 'Paules, Catharine (NIH/NIAID) [E]' <catharine.paules@nih.gov>; 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; 'Cozart, Barbara (CDC/OID/NCIRD)'

<wjn4@cdc.gov>

**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Final submission attached

Final submission attached for your records.

I spoke to Bill Beck, the Pharmaceutical Sciences Section Secretary -- and he has agreed to endorse our submission.

Thank you!

Karen

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL (b)(6) (b)(6)

**From:** Chandross, Karen /US

**Sent:** Monday, April 16, 2018 11:16 AM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; (b)(6)

(b)(6); Nabel, Gary /US (b)(6)

**Cc:** 'Baltimore, David' <baltimo@caltech.edu>; Wei, Ronnie /US (b)(6)

Travayiakis, Carol /US <(b)(6)>; 'Conrad, Patricia (NIH/NIAID) [E]'

<conradpa@niaid.nih.gov>; Cozart, Barbara (CDC/OID/NCIRD) <wjn4@cdc.gov>

**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation -- all proposed participants confirmed -- please send title & 2-3 sentence description

**Importance:** High

Dear All – thank you for agreeing to participate in a proposed 2019 AAAS session, which focuses on addressing *The quest for a universal flu vaccine*.

We are very excited to have a great line up and, if selected, David Baltimore has kindly agreed to serve as moderator.

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

Keeping in mind the April 19<sup>th</sup> submission deadline, for our speakers, I must submit a 1) a **title for your talk** and 2) **up to 3 short sentences that describes your focus**-- if you would send this to me at your earlier convenience.

Please note that we would plan to have short talks followed by a longer panel discussion that also includes engaging the audience.

All the best,

Karen

**Info:**

1. 2019 AAAS meeting (February 14-18) in Washington, DC.
2. In line with AAAS's interest in topics with broad appeal and relevancy, we are submitting a proposal for a 90-min symposium (<https://aaas.confex.com/aaas/2019/symp90/cfp.cgi>) on "*The quest for a universal flu vaccine.*"
3. Theme is "*Science Transcending Boundaries,*" which offers an opportunity to bridge the gap between scholar and practitioner and leverage expertise from different disciplines to highlight the greatest challenges and most promising solutions to achieving an impactful solution.
4. For the session format, 3 speakers are asked to give presentations (~20 minutes each), followed by a ~30 minute Q&A period with the audience.

**The quest for a universal flu vaccine**

According to the World Health Organization, seasonal influenza epidemics cause 3 to 5 million severe cases and 300,000 to 500,000 deaths globally each year. In the United States alone, there are 140,000 to 710,000 influenza-related hospitalizations and 12,000 to 56,000 deaths each year, with the highest burden of disease affecting the very young, the very old, and people with coexisting medical conditions. The most recent 2017/2018 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

**Moderator:** David Baltimore, PhD

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

**Organizer:** Karen Chandross, PhD, Sanofi R&D

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) | CELL: (b)(6) (b)(6)



**From:** aaas@confex.com  
**Sent:** Tue, 10 Jul 2018 20:56:24 +0000  
**To:** (b)(6)  
**Subject:** [EXTERNAL] AAAS 2019 Annual Meeting Proposal Decision (Session ID #21433)



Dear Karen Chandross, PhD,

I am pleased to inform you that your proposal, ID# 21433 "The quest for a universal flu vaccine," has been accepted by the Program Committee for the 2019 AAAS Annual Meeting, to be held February 14-17 in Washington, DC. Please inform your panelists as soon as possible, and ask them to check their passports and international travel requirements if needed.

As the organizer, you are the primary contact for your session, and will be responsible for disseminating relevant material to your participants.

Please ask your panelists if they have any scheduling restrictions for Friday, February 15 through Sunday, February 17, 2019. The schedules of nearly 1,000 panelists must be coordinated and cross-checked against other variables in order to set the program schedule. **Please email scheduling restrictions for the panel to [meetings@aaas.org](mailto:meetings@aaas.org) no later than Tuesday, July 24, and include the session ID number and title in the email subject line.**

On August 1, panel participants will be contacted directly by AAAS and asked to confirm their participation in your session. Speakers will also be asked to review their presentation titles, submit any conflict-of-interest information, complete recording waivers, and later to submit lay-language summaries of their talks. Please inform me about changes to your session as soon as they occur (for example, if any of the speakers have changed).

Below is a brief summary of what to expect in the coming months:

- Early August: All participants will receive information about registration and housing when these sites open online. **To register with the reduced rate, participants must use the link that will be emailed to them from Experient, the AAAS registration service provider.**
- Early September: Information about applying for travel support will be sent only to you (the organizer), with further instructions for informing your panelists.
- Late September: Session organizers will receive information about their session's date and time assignment.
- Early October: The meeting program and schedule will be posted online, with the exception of session rooms.
- Early January: Current registrants will be asked to indicate the sessions in which they are most interested. This feedback will help guide room assignments.
- Early February: Session rooms will be posted.

If you proposed more than one session, you will receive separate notification(s) for each. Please make sure that you can receive email from: [agreene@aaas.org](mailto:agreene@aaas.org), [cjones@aaas.org](mailto:cjones@aaas.org), [nmaylett@aaas.org](mailto:nmaylett@aaas.org), [kklyberg@aaas.org](mailto:kklyberg@aaas.org), [jstevens@aaas.org](mailto:jstevens@aaas.org), and [meetings@aaas.org](mailto:meetings@aaas.org).

If you have any questions, please contact me at [agreene@aaas.org](mailto:agreene@aaas.org) or 202-326-6593.

Sincerely,

**Ashira B. Greene, Ph.D.**

Program Associate

**AAAS Annual Meeting**

February 14-17, 2019 • Washington, DC

[www.aaas.org/meetings](http://www.aaas.org/meetings)



## SESSION SUBMITTED FOR REVIEW

---

Click [here](#) to print this page now.

**You have submitted the following session to 2019 Annual Meeting.** Receipt of this notice does not guarantee that your submission was complete, free of errors, or accepted for presentation.

---

### The quest for a universal flu vaccine

The quest for a universal flu vaccine

**Submitter's Email:**

(b)(6)

**Session Type:**

90 Minute Symposium Format

**Session Description:**

Seasonal influenza epidemics cause 3-5 million severe cases and up to 500K deaths globally each year. In the US alone, there are 140K-710K influenza-related hospitalizations and 12K-56K deaths each year, with the highest burden of disease affecting the very young, the very old and people with coexisting medical conditions. The most recent 2017-18 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

**Categories:**

1. Health and Pharmaceutical Science
2. Global Perspectives and Issues

**Section Member Affiliation:**

Pharmaceutical Sciences (S)

**Relevance to Theme or Special Relevance to the Audience:**

Bridging the gap between scholar and practitioner and leverage expertise from different disciplines: Pharma (private sector), National Institutes of Health (NIH), and the Centers for Disease Control and Prevention, and National Center for Immunization and Respiratory Diseases (CDC-NCIRD), to span the breadth from innovative research to product development and global access, discuss the greatest challenges and most promising approaches, and collaborative opportunities aimed at achieving an impactful, timely solution.

**Disciplinary Sections Consulted?**

Yes

**If so, which sections were consulted?**

- Pharmaceutical Sciences (S)

**Anything to disclose?**

No

**Diversity Statement:**

Well-balanced, cross disciplinary session with senior level professional participants from both the private (Pharma) and public (NIH, CDC) sectors, coming from different cultural backgrounds and with the inclusion of women as key contributors (session organizer, speaker).

**Sections:**

- MEDICAL SCIENCES
- PHARMACEUTICAL SCIENCES
- SOCIETAL IMPACTS OF SCIENCE AND ENGINEERING

**keywords:**

biomedical research (clinical), biomedical research (preclinical), disease prevention, global and public health and infectious disease

---

**Moderator**

David Baltimore, PhD  
President Emeritus; Robert Andrews Millikan Professor of Biology  
Caltech  
1200 East California Blvd  
Mail Code 147-75  
Pasadena, CA  
USA  
**Phone Number:** (b)(6)  
**Email:** baltimo@caltech.edu

---

**Organizer**

Karen Chandross, PhD  
Senior Director, R&D  
Sanofi  
55 Corporate Drive  
Bridgewater, NJ  
USA  
**Phone Number:** (b)(6)  
**Email:** (b)(6)



---

Speaker

---

Gary J. Nabel, MD, PhD  
Chief Scientific Officer  
Sanofi  
640 Memorial Drive  
Room 5951A  
Cambridge, MA  
USA

**Phone Number:** (b)(6)

**Email:** (b)(6)

**Title:** Rational Design and Development of Universal Influenza Vaccines

**Talk Description:** This talk will cover the alternative paths to improved influenza vaccines. Different potential approaches to a broadly protective antibody will be highlighted. Major scientific challenges and opportunities based on influenza biology and the human immune response will be discussed. Finally, considerations for product development will be reviewed, including clinical testing, regulatory, and manufacturing issues, as well as opportunities to advance through public-private partnerships.

**Status:** Confirmed

---

Speaker

---

Anthony Fauci, MD  
Director  
NIH, National Institute of Allergy and Infectious Disease (NIAID)  
31 Center Drive  
Building 31, Room 7A03  
Bethesda, MD  
USA

**Phone Number:** (b)(6)

**Email:** (b)(6)

**Title:** Chasing Influenza: The Need for a Universal Influenza Vaccine

**Talk Description:** Strain-specific vaccination for influenza is suboptimal: 1) Seasonal vaccines are not consistently effective 2) Pandemics occur and response after the fact is ineffective 3) chasing after potential pandemic viruses is costly and ineffective. Our goal is a universal influenza vaccine that would protect against both seasonal and pandemic viruses. To achieve this, we must improve production strategies for influenza vaccines and advance from strain-specific to universal strain coverage.

**Status:** Confirmed

---

Speaker

---

Nancy Messonnier, MD  
Director  
National Center for Immunization and Respiratory Diseases, CDC-  
OID  
1600 Clifton Road  
MS A-27  
Atlanta, GA  
USA

**Phone Number:** 404.639.4734

**Email:** nar5@cdc.gov

**Title:** Hit Me With Your Best Shot: Before and After a Universal Flu Vaccine

**Talk Description:** While the promise of a universal flu vaccine may be years in the future, how can we reduce flu burden until one is developed and what ground work can we lay in advance? As we track domestic and international surveillance trends and learn more about how flu works and our response to it, we have to improve our current vaccines and evaluate if different types of vaccine are more beneficial. Data tells us that flu vaccine coverage is linked to how well the vaccine works. Working to ensure the current vaccines are effective and safe before we have a universal vaccine can pave the way for its acceptance.

**Status:** Confirmed

---

**1. IF NECESSARY, PLEASE CHANGE YOUR SESSION INFORMATION BETWEEN NOW AND THE DEADLINE OF Thursday, April 19, 2018.**

- Point your browser to the URL that has been sent to you via email

Any changes that you make will be reflected instantly in what is seen by the reviewers. You do NOT need to go through all of the submission steps in order to change one thing. If you want to change the title, for example, just click "Title" in the Control Panel and submit the new title. You can close your browser, or browse to some other web site, as soon as you have submitted the change.

[Tell us what you think of online session submittal.](#)

Tell us what you liked or what we need to improve and we'll work on new features for future meetings.

<http://aaas.org>

**From:** (b)(6)  
**Sent:** Fri, 13 Jul 2018 16:28:18 +0000  
**To:** (b)(6); baltimo@caltech.edu; Messonnier, Nancy (CDC/OID/NCIRD) (b)(6)  
**Cc:** (b)(6); catharine.paules@nih.gov; Conrad, Patricia (NIH/NIAID) [E]; Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Session Accepted

Based on your quick responses, I'll let the AAAS know that there is a conflict on Feb 15<sup>th</sup> – but none for Feb 16 and 17<sup>th</sup>.

Thank you.  
Karen

**From:** Nabel, Gary /US  
**Sent:** Wednesday, July 11, 2018 12:19 PM  
**To:** Chandross, Karen /US (b)(6); Baltimore, David <baltimo@caltech.edu>; Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>; (b)(6)  
**Cc:** Wei, Ronnie /US (b)(6); Travayiakis, Carol /US (b)(6); Paules, Catharine (NIH/NIAID) [E] <catharine.paules@nih.gov>; Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Cozart, Barbara (CDC/OID/NCIRD) <wjn4@cdc.gov>  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Session Accepted

Hi Karen,  
Congratulations on this positive response!  
It's nice to see the interest in this important topic.

I am available to join on any day with the possible exception of Friday Feb 15 because I will be speaking at a Keystone meeting.

If it becomes problematic, I can work with the organizers to speak earlier in the meeting. But for the moment, it represents a potential conflict.

Thanks for your hard work in putting the proposal together. I look forward to participating.

Best  
Gary

**From:** Chandross, Karen /US  
**Sent:** Tuesday, July 10, 2018 8:17 PM  
**To:** Nabel, Gary /US (b)(6); 'Baltimore, David' <baltimo@caltech.edu>; 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; (b)(6)  
**Cc:** Wei, Ronnie /US (b)(6); Travayiakis, Carol /US (b)(6); 'Paules, Catharine (NIH/NIAID) [E]' <catharine.paules@nih.gov>; 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; 'Cozart, Barbara (CDC/OID/NCIRD)'



<wjn4@cdc.gov>

**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Session Accepted

Dear Gary, David, Nancy and Anthony,

I am excited to share that our Universal Flu session proposal was accepted by the AAAS review committee!

Attached is the email I received today – and a copy of our submission.

As a first step, AAAS is asking if you have any scheduling restrictions from Friday, Feb 15 through Sun, Feb 17, 2019. If you would **send me any conflicts by July 23<sup>rd</sup>**, then I'll consolidate and follow-up with the coordinators.

AAAS will reach out to you directly on Aug 1<sup>st</sup> -- to confirm your participation, review your presentation title and complete some paperwork -- if you can keep an eye out for that email.

Looking forward to the opportunity to work together to create an impactful session!

Best,  
Karen

**Karen CHANDROSS, PhD**

**Strategic Initiatives & Scientific Relations  
Program Director, iDEA awards**

Sanofi R&D

TEL: (b)(6) | CELL: (b)(6) | (b)(6)

**From:** Chandross, Karen /US

**Sent:** Thursday, April 19, 2018 1:53 PM

**To:** 'Baltimore, David' <baltimo@caltech.edu>; 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>;

(b)(6); (b)(4); Nabel, Gary /US <(b)(6)>

**Cc:** Wei, Ronnie /US <(b)(6)>; Travayiakis, Carol /US

(b)(6); 'Paules, Catharine (NIH/NIAID) [E]' <catharine.paules@nih.gov>;

'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; 'Cozart, Barbara (CDC/OID/NCIRD)'

<wjn4@cdc.gov>

**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Final submission attached

Final submission attached for your records.

I spoke to Bill Beck, the Pharmaceutical Sciences Section Secretary -- and he has agreed to endorse our submission.

Thank you!  
Karen

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL: (b)(6) | (b)(6)

**From:** Chandross, Karen /US

**Sent:** Monday, April 16, 2018 11:16 AM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <[nar5@cdc.gov](mailto:nar5@cdc.gov)> (b)(6)

(b)(6); Nabel, Gary /US (b)(6)

**Cc:** 'Baltimore, David' <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; Wei, Ronnie /U (b)(6)

Travayiakis, Carol /US (b)(6); 'Conrad, Patricia (NIH/NIAID) [E]'

<[conradpa@niaid.nih.gov](mailto:conradpa@niaid.nih.gov)>; Cozart, Barbara (CDC/OID/NCIRD) <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>

**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation -- all proposed participants confirmed -- please send title & 2-3 sentence description

**Importance:** High

Dear All – thank you for agreeing to participate in a proposed 2019 AAAS session, which focuses on addressing *The quest for a universal flu vaccine*.

We are very excited to have a great line up and, if selected, David Baltimore has kindly agreed to serve as moderator.

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

Keeping in mind the April 19<sup>th</sup> submission deadline, for our speakers, I must submit a 1) a **title for your talk** and 2) **up to 3 short sentences that describes your focus**-- if you would send this to me at your earlier convenience.

Please note that we would plan to have short talks followed by a longer panel discussion that also includes engaging the audience.

All the best,  
Karen

**Info:**

1. 2019 AAAS meeting (February 14-18) in Washington, DC.
2. In line with AAAS's interest in topics with broad appeal and relevancy, we are submitting a proposal for a 90-min symposium (<https://aaas.confex.com/aaas/2019/symp90/cfp.cgi>) on "*The quest for a universal flu vaccine*."

3. Theme is “*Science Transcending Boundaries*,” which offers an opportunity to bridge the gap between scholar and practitioner and leverage expertise from different disciplines to highlight the greatest challenges and most promising solutions to achieving an impactful solution.
4. For the session format, 3 speakers are asked to give presentations (~20 minutes each), followed by a ~30 minute Q&A period with the audience.

### **The quest for a universal flu vaccine**

According to the World Health Organization, seasonal influenza epidemics cause 3 to 5 million severe cases and 300,000 to 500,000 deaths globally each year. In the United States alone, there are 140,000 to 710,000 influenza-related hospitalizations and 12,000 to 56,000 deaths each year, with the highest burden of disease affecting the very young, the very old, and people with coexisting medical conditions. The most recent 2017/2018 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

**Moderator:** David Baltimore, PhD

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

**Organizer:** Karen Chandross, PhD, Sanofi R&D

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL: (b)(6) (b)(6)

**From:** Grabenstein, John D.  
**Sent:** Fri, 22 Jun 2018 20:10:46 +0000  
**To:** Cohn, Amanda (CDC/OID/NCIRD); Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Collier, Beth-Ann Griswold; Mahon, Barbara (CDC/OID/NCIRD); Silsbee, Jeffrey C  
**Subject:** Ebola Vaccine filing status

CAPT Cohn, Dr. Messonnier,

Congratulations on another successful ACIP meeting this week. Yours is the only NITAG in the world that I know of that is conducted in public, not to mention broadcast to the world on the Internet.

When we met in Atlanta last June, CAPT Cohn, you indicated that you may wish to begin forming an ACIP work group to assess candidate Ebola vaccines ~ 12 to 18 months before anticipated licensure by the FDA.

(b)(4)

When it is convenient, we would be happy to discuss what kind of timing you would like for presentations of our V920 clinical-development program and the preclinical and clinical evidence already in hand.

I will serve as your principal point of contact, helping you engage with Merck's world-class scientific experts.

At the same time, we appreciate all the scientific expertise CDC brings to Ebola prevention and response. We wish safe travels to all the CDC team members in and around the outbreak and investigation zones in central Africa.

Respectfully, John

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Research Laboratories  
351 N. Sumneytown Pike, UG-2B09  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.



**From:** (b)(6)  
**Sent:** Fri, 3 Aug 2018 14:36:59 +0000  
**To:** Cohn, Amanda (CDC/OID/NCIRD); Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** RE: Redfield flu discussion

Thanks Amanda –

(b)(6)

Could we do the week after? Could something between 9 and noon on 8/23 work?

Julian

---

**From:** Cohn, Amanda (CDC/OID/NCIRD) [mailto:anc0@cdc.gov]  
**Sent:** Friday, August 03, 2018 10:31 AM  
**To:** Ritchey, Julian /US; Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** [EXTERNAL] RE: Redfield flu discussion

Julian,

I apologize for not following up. Are you available to talk the week of August 13<sup>th</sup>? I think you and I can touch base and if we need to loop Nancy in at all I can do that after we talk.

Thanks!  
Amanda

---

**From:** Julian.Ritchey@sanofi.com <(b)(6)>  
**Sent:** Friday, August 3, 2018 12:58 AM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD) <nar5@cdc.gov>  
**Cc:** Cohn, Amanda (CDC/OID/NCIRD) <anc0@cdc.gov>  
**Subject:** RE: Redfield flu discussion

Hello again –

Following up on the note below to see how we can help with the various facets of flu that are under foot.

Please let us know how we can be of help.

Julian

---

**From:** Ritchey, Julian /US  
**Sent:** Tuesday, July 10, 2018 5:31 PM  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Cohn, Amanda (CDC/OID/NCIRD)  
**Subject:** RE: Redfield flu discussion

Dear both –

Thank you both for your notes.

It would be great to connect to hear plans for the forums, the kind of information you are looking to gather, and discuss seasonal opportunities.

Nancy, Angie Bricco from my team mentioned the two of you had spoken at NIC about some of the vaccine confidence work she has been doing.

Could the 4 of us connect on these areas and understand how we can contribute to Dr. Redfield's efforts?

As I'm in France next week, would Friday 7/20 at 10 or 11am ET be feasible?

Julian

---

**From:** Messonnier, Nancy (CDC/OID/NCIRD) [<mailto:nar5@cdc.gov>]

**Sent:** Tuesday, July 10, 2018 4:53 PM

**To:** Ritchey, Julian /US

**Cc:** Cohn, Amanda (CDC/OID/NCIRD)

**Subject:** [EXTERNAL] RE: Redfield flu discussion

Julian,

I appreciate the email and your reaching out. Amanda was going to touch base with you to get your input into forums with Dr. Redfield, especially around vaccine development. Equally, I'd definitely be happy to discuss with you opportunities with the currently available vaccines.

Nancy

---

**From:** (b)(6)

**Sent:** Monday, July 9, 2018 11:19 AM

**To:** Messonnier, Nancy (CDC/OID/NCIRD) <[nar5@cdc.gov](mailto:nar5@cdc.gov)>

**Subject:** Redfield flu discussion

Dear Nancy –

I am reaching to share with you a conversation several of us at Sanofi Pasteur had with Dr. Redfield this past Friday in case you are not already aware of it. At its root, an invitation to further discussion and exploration, Dr. Redfield is interested in coordinating internal briefings with external perspectives on addressing the future course of flu vaccines. In addition to the technologic questions he had, I found it both interesting and encouraging that he recognizes and plans to emphasize the importance of seasonal vaccination coverage as an immediate step that can be taken while the longer term, more sensational solutions are pursued.

He indicated he plans follow-up meetings on this both across industry and in bilateral forums, so I wanted to touch base with you to offer any assistance I can on behalf of Sanofi Pasteur as I see this as a great opportunity for increased attention on multiple levels for the work that NCIRD is doing to reframe the severity of flu and to drive seasonal immunization—key opportunities in the face of the VE challenges of this past season and the hype of universal vaccines.



Please let me know if we could connect to discuss this and/or our advocacy approach to flu for this coming season as I believe this attention is a great opportunity for addressing many of the challenges present in the flu market.

Be well –  
Julian

**From:** (b)(6)  
**Sent:** Wed, 8 Aug 2018 14:48:22 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD); Cozart, Barbara (CDC/OID/NCIRD); (b)(6); Conrad, Patricia (NIH/NIAID) [E]; baltimo@caltech.edu; (b)(6)  
**Cc:** (b)(6)  
**Subject:** 2019 AAAS Annual Meeting - Registration & hotel

I just walked through the process – and determined that you cannot book hotel without registering for the meeting. The schedule will be announced in early October, so you can either wait until then or you can just pick a date within the meeting time frame and add to the registration and hotel reservation and then edit as needed when the schedule is announced.

Best,  
Karen

**From:** Chandross, Karen /US  
**Sent:** Monday, August 6, 2018 9:21 AM  
**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; 'Cozart, Barbara (CDC/OID/NCIRD)' <wjn4@cdc.gov>; (b)(6); 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; 'Baltimore, David' <baltimo@caltech.edu>; Nabel, Gary /US; (b)(6)  
**Cc:** Wei, Ronnie /US <Ronnie.Wei2@sanofi.com>; Travayiakis, Carol /US; (b)(6)  
**Subject:** FW: [EXTERNAL] 2019 AAAS Annual Meeting - Registration notification

Dear Colleagues,

As an update, I received the following AAAS meeting registration email. **Please let me know if you have not yet received something similar.**

Although I requested Sat, Feb 16<sup>th</sup> -- we do not yet know our session date. As such, please wait to register unless you plan to attend the full 3-day meeting. The organizers also suggest booking your hotel asap – keeping in mind cancellation policies (in case of the need to modify).

The **scientific sessions** will be held at the Washington **Marriott Wardman Park Hotel** (260 Woodley Rd, NW).

**Hotel and travel information** is available on the AAAS Annual Meeting website:

<http://meetings.aaas.org/travel>

Special **AAAS hotel rates** are only available through the meeting registration website **until January 22, 2019.**

I'll reach out again once we have the session date confirmed.

Best,  
Karen

Karen CHANDROSS, PhD

Strategic Initiatives & Scientific Relations

Program Director, iDEA awards

Sanofi R&D

TEL: (b)(6) | CELL: (b)(6) | (b)(6)

---

**From:** AAAS Annual Meeting [[mailto:email\\_confirm@confmail.experient-inc.com](mailto:email_confirm@confmail.experient-inc.com)]

**Sent:** Friday, August 3, 2018 8:25 AM

**To:** Chandross, Karen /US (b)(6)

**Subject:** [EXTERNAL] 2019 AAAS Annual Meeting - Complete your registration {AAA191:1274}



\*\*\* Please do not reply to this e-mail. It was sent from an automated system. \*\*\*

## 2019 AAAS Annual Meeting Registration

Dear Karen Chandross, PhD,

The following information will guide you in registering and reserving a hotel room for the 2019 AAAS Annual Meeting in Washington, DC (February 14-17).

Scientific session and workshop participants may register for the full conference at these deeply discounted rates:

\$120 Discounted Panelist Rate for Full Meeting

\$-0- Panelist attendance for 1 day only (the day of your session).

Offer not available if you are speaking on 2 or more days.

The schedule for sessions and workshops will be available online in early October.

*If you are registering just for one day, you may prefer to register once the meeting schedule is available.*

## Registration Instructions

[Click here to access your registration.](#)

# Profile

Confirmation ID: 1274  
Karen Chandross, PhD  
Sanofi  
55 Corporate Drive  
Bridgewater, NJ 08807

*Note: If you are a AAAS staff member, AAAS Section Officer (secretary, chair, retiring-chair, or chair-elect), Council Member, or Section Member-At-Large, you will receive a separate set of instructions and special log-in information to register and make your hotel reservation.*

## AAAS Annual Meeting scientific sessions will take place at:

**Washington Marriott Wardman Park Hotel** ([2660 Woodley Rd, NW](#))

Special AAAS hotel rates are only available through the meeting registration website until **January 22, 2019**. You are encouraged to make your reservation as soon as possible, as rooms are assigned on a first-come, first-served basis and may sell out prior to the deadline. Do not contact the hotels directly to make your reservation.

Hotel and travel information is available on the AAAS Annual Meeting website:

<http://meetings.aaas.org/travel>

*You may be contacted by companies not affiliated with AAAS to book your hotel rooms at supposedly significant discounts.* Reservations made through one of these companies will be at your own risk, and AAAS will not take responsibility for any lost deposits, reservation relocation, or accuracy in type of room reserved. If you are contacted by another housing company trying to sell hotel rooms, please notify [kklyberg@aaas.org](mailto:kklyberg@aaas.org) or (202) 326-6214.

If you have any questions or need more information, please feel free to contact me.

Best,

Kim Klyberg  
Senior Meetings and Special Events Associate  
AAAS – American Association for the Advancement of Science

1200 New York Avenue, NW  
Washington, DC 20005  
P: 202-326-6214  
E: [kklyberg@aaas.org](mailto:kklyberg@aaas.org)

[Experient Privacy Policy](#) | [Experient Terms of Use](#)

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

**From:** (b)(6)  
**Sent:** Wed, 5 Sep 2018 15:10:21 +0000  
**To:** abjohnson@aaas.org; (b)(6) Messonnier, Nancy  
(CDC/OID/NCIRD); (b)(6)  
**Cc:** baltimo@caltech.edu; Carol (b)(6) Cozart, Barbara  
(CDC/OID/NCIRD); Conrad, Patricia (NIH/NIAID) [E]; Hoffman, Hillary (NIH/NIAID)  
[E]; (b)(6)  
**Subject:** RE: 2019 AAAS Annual Meeting: Possible news briefing for "The Quest for a Universal Flu Vaccine"

Dear Amanda, thank you for reaching out to us about the AAAS press briefings opportunity.

I would like to confirm that Gary Nabel is available to speak to you on Sept 10<sup>th</sup> at 10 am and, as our Chief Scientific Officer, he can represent Sanofi's latest research efforts. Please copy Carol Travayiakis, who can help in arranging this meeting.

In addition to Drs. Nabel, Fauci and Messonnier – I'd like to suggest also reaching out to Dr. David Baltimore (in copy), who will be moderating our session.

Perhaps you and I should touch base after you have spoken to each of the speakers in our Flu session – if you would like to propose any time after 1 pm on Sept 10th. If, after your individual meetings, you think it would be worth having a discussion with all speakers together, then we can work on this.

Best regards,  
Karen

**Karen CHANDROSS, PhD**

**Strategic Initiatives & Scientific Relations**

**Program Director, iDEA awards**

Sanofi R&D

TEL: (b)(6) CELL: (b)(6) | (b)(6)

**From:** Amanda B Johnson [mailto:abjohnson@aaas.org]  
**Sent:** Tuesday, September 4, 2018 2:58 PM  
**To:** Chandross, Karen /US <(b)(6)>; Nabel, Gary /US <(b)(6)>  
<(b)(6)> <Anthony.fauci@nih.gov>; 'nar5@cdc.gov' <nar5@cdc.gov>  
**Cc:** Robinson, Anna /FR <(b)(6)>; 'hillary.hoffman@nih.gov'  
<hillary.hoffman@nih.gov>  
**Subject:** [EXTERNAL] 2019 AAAS Annual Meeting: Possible news briefing for "The Quest for a Universal Flu Vaccine"

Dear Drs. Chandross, Nabel, Fauci, and Messonnier:



My name is Amanda Johnson, and in advance of the AAAS Annual Meeting in February, I am working with a small committee here at AAAS to investigate which approved Annual Meeting symposia might be suitable for an additional Annual Meeting event – a **AAAS Annual Meeting press briefing**.

Press briefings at the Annual Meeting entail 45-minute sessions in which each of a symposium's speakers shares **\*new\*** research related to their field, followed by a 20-30 minute Q&A with reporters. (The Annual Meeting typically draws about 500 reporters who attend the briefings to ask good questions and write about the related work in popular outlets including The Associated Press, *The Washington Post*, and *The New York Times*.)

Your symposium, **The Quest for a Universal Flu Vaccine**, looks quite promising for a news briefing. To that end, I wanted to reach out to you to see if each confirmed speaker (**Drs. Nabel, Fauci, and Messonnier**, if I'm understanding correctly) might have time to talk with me about your most recent research efforts (again, a critical criteria for a symposium to be selected for a press briefing is for new, previously undisclosed research/sentiments/trends to be among the discussion points — creating a "news hook" for reporters).

I will report to my committee in mid-September so it would be terrific to talk with each of you, if you have the time, for about 15 minutes, respectively, before that time. Below my signature, in yellow, I propose individual times, for your consideration. Alternatively, I would be happy to suggest a conference call time, where we all could connect at once. If that is appealing, might you all (**Drs. Nabel, Fauci, and Messonnier** and **Dr. Chandross**, too, as the organizer) be available at 2:00 pm am ET on Monday, 10 September? Or, if you prefer the individually listed times, below, we could go that route, too.

I'm looking forward to talking with you all.

Best,  
Amanda

**Dr. Chandross:** (as the organizer, your insights would be most valuable, too, if time permits): might you be available at 9:00 am ET on Monday, 10 Sept?

**Dr. Nabel:** might you be available at 10:00 am ET on Monday, 10 Sept?

**Dr. Fauci:** might you be available at 11:00 am ET on Monday, 10 Sept?

**Dr. Messonnier:** might you be available at 1:00 pm ET on Monday, 10 Sept?

**Amanda Johnson, PhD**, Science Press Package Deputy Director  
American Association for the Advancement of Science (AAAS)  
1200 New York Avenue, NW | Washington, DC 20005  
Ph: 202-326-7088

E-mail: [abjohnson@aaas.org](mailto:abjohnson@aaas.org)

Follow "SciPak" on [Twitter](#)



**From:** Bresnitz, Eddy A.  
**Sent:** Wed, 24 Oct 2018 19:15:35 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD)  
**Subject:** RE: Adenovirus outbreak

Thanks Nancy; Will pass this on right now. Eddy

-----Original Message-----

From: Messonnier, Nancy (CDC/DDID/NCIRD) <nar5@cdc.gov>  
Sent: Wednesday, October 24, 2018 3:14 PM  
To: Bresnitz, Eddy A. (b)(6)  
Subject: Re: Adenovirus outbreak

EXTERNAL EMAIL – Use caution with any links or file attachments.

Congressman Freylinghusen is the member that contacted us.

> On Oct 24, 2018, at 2:12 PM, Bresnitz, Eddy A. (b)(6) wrote:

>  
>

> Nancy, NJ would like the name of the congressman and the health  
> commissioner will reach out to him/her directly. FYI, apparently the  
> governor is planning to hold a press conference this afternoon with  
> the health commissioner about this outbreak. Eddy

>

> Sent from my iPhone

> Notice: This e-mail message, together with any attachments, contains  
> information of Merck & Co., Inc. (2000 Galloping Hill Road,  
> Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct  
> contact information for affiliates is available at  
> <http://www.merck.com/contact/contacts.html> that may be confidential,  
> proprietary copyrighted and/or legally privileged. It is intended  
> solely for the use of the individual or entity named on this message.  
> If you are not the intended recipient, and have received this message  
> in error, please notify us immediately by reply e-mail and then delete  
> it from your system.

>

Notice: This e-mail message, together with any attachments, contains  
information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth,  
New Jersey, USA 07033), and/or its affiliates Direct contact information  
for affiliates is available at  
<http://www.merck.com/contact/contacts.html> that may be confidential,  
proprietary copyrighted and/or legally privileged. It is intended solely  
for the use of the individual or entity named on this message. If you are  
not the intended recipient, and have received this message in error,  
please notify us immediately by reply e-mail and then delete it from  
your system.

**From:** Bresnitz, Eddy A.  
**Sent:** Thu, 25 Oct 2018 18:32:33 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD)  
**Subject:** FW: [EXTERNAL] Adenovirus outbreak

Nancy: FYI. Eddy

---

**From:** Tan, Christina G <Christina.Tan@doh.nj.gov>  
**Sent:** Thursday, October 25, 2018 12:54 PM  
**To:** Bresnitz, Eddy A. (b)(6)  
**Cc:** Leusner, Donna M <Donna.Leusner@doh.nj.gov>; Montana, Barbara <Barbara.Montana@doh.nj.gov>  
**Subject:** RE: [EXTERNAL] Adenovirus outbreak [Confidential]

**EXTERNAL EMAIL** – Use caution with any links or file attachments.

Hi Eddy—

The Commissioner said he will be calling Frelinghusen this morning.

Tina Tan, MD, MPH  
State Epidemiologist/Assistant Commissioner  
Division of Epidemiology, Environmental and Occupational Health  
New Jersey Department of Health  
135 E. State Street  
PO Box 369  
Trenton, NJ 08625-0360  
Office: (609) 826-5967  
Fax: (609) 826-4750  
[christina.tan@doh.nj.gov](mailto:christina.tan@doh.nj.gov)

system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Grabenstein, John D.  
**Sent:** Fri, 26 Oct 2018 21:21:11 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD); Cohn, Amanda (CDC/DDID/NCIRD)  
**Subject:** FW: NYTimes.com: Bruno Latour, the Post-Truth Philosopher, Mounts a Defense of Science

This is a long article about a philosopher of science. There is a brief mention about vaccine skepticism at the beginning, but most of the references involve climate change.

Even so, this paragraph stood out for me...

“At a meeting between French industrialists and a climatologist a few years ago, Latour was struck when he heard the scientist defend his results not on the basis of the unimpeachable authority of science but by laying out to his audience his manufacturing secrets: “the large number of researchers involved in climate analysis, the complex system for verifying data, the articles and reports, the principle of peer evaluation, the vast network of weather stations, floating weather buoys, satellites and computers that ensure the flow of information.” The climate denials, by contrast, the scientist said, had none of this institutional architecture. Latour realized he was witnessing the beginnings a seismic rhetorical shift: from scientists appealing to transcendent, capital-T Truth to touting the robust networks through which truth is, and has always been, established.”

For what it's worth....

John

---

**From:** Grabenstein, John D.  
**Sent:** Friday, October 26, 2018 17:18  
**To:** Grabenstein, John D.; (b)(6)  
**Subject:** NYTimes.com: Bruno Latour, the Post-Truth Philosopher, Mounts a Defense of Science

From The New York Times:

Bruno Latour, the Post-Truth Philosopher, Mounts a Defense of Science

He spent decades deconstructing the ways that scientists claim their authority. Can his ideas help them regain that authority today?

<https://www.nytimes.com/2018/10/25/magazine/bruno-latour-post-truth-philosopher-science.html>

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Ignas-Badman, Karen  
**Sent:** Mon, 22 Oct 2018 16:13:49 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD)  
**Cc:** 'anc0@cdc.gov'; ROMEROJOSE@UAMS.EDU'; PSzilagyi@mednet.ucla.edu'; lem2@cdc.gov'; hbc7@cdc.gov'; Kuter, Barbara J.  
**Subject:** FW: 9vHPV - Use in 27-45 Year Olds - Background for October 25, 2018 ACIP meeting  
**Attachments:** HPV - Letter to HPV WG ACIP - 22-Oct-2018.pdf, HPV Summary Document-ACIP 27-45 year olds.pdf, HPV Appendix-ACIP 27-45 year olds.pdf

Dear Dr. Messonnier,  
I am resending the e-mail below to you as its initial distribution did not contain your complete e-mail address.

Sincerely,  
Karen

---

**From:** Ignas-Badman, Karen **On Behalf Of** Barr, Eliav  
**Sent:** Monday, October 22, 2018 10:37 AM  
**To:** 'nar@cdc.gov'; 'anc0@cdc.gov'  
**Cc:** 'ROMEROJOSE@UAMS.EDU'; 'PSzilagyi@mednet.ucla.edu'; 'lem2@cdc.gov'; 'hbc7@cdc.gov'; Kuter, Barbara J.  
**Subject:** 9vHPV - Use in 27-45 Year Olds - Background for October 25, 2018 ACIP meeting

Dear Drs. Messonnier and Cohn,  
We would greatly appreciate if you would distribute the attached letter and two supporting documents to the HPV Work Group, relevant members of the CDC staff, each ACIP member, and each liaison member. It is important that this be done within the next 1-2 days so that these individuals have the opportunity to review the materials in advance of the October 25, 2018 ACIP discussion on HPV vaccine.

Many thanks!

Sincerely,  
Eliav

*Eliav Barr, SVP and Head / Merck Research Laboratories / MRL Global Medical Affairs / Mail Stop UG4CD-08, 351 N. Sumneytown Pike, North Wales, PA 19454, USA /*

(b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information

for affiliates is available at  
<http://www.merck.com/contact/contacts.html>) that may be confidential,  
proprietary copyrighted and/or legally privileged. It is intended solely  
for the use of the individual or entity named on this message. If you are  
not the intended recipient, and have received this message in error,  
please notify us immediately by reply e-mail and then delete it from  
your system.

(b)(4)



(b)(4)

## **Summary of the Need for HPV Vaccination in Mid-Adult Persons 27-45 Years of Age, and Differences in Cost-effectiveness Models Presented at October 2018 ACIP**

### ***Background***

Based on a significant unmet medical need for protection against HPV among mid-adult persons (MAPs) 27 through 45 years of age, the FDA recently granted priority review for Merck's application to extend the upper age indication of the nine-valent human papillomavirus (9vHPV) vaccine from 26 to 45 years. Based on the strong evidence provided in the application, including a substantial event rate for HPV disease among placebo recipients in the Phase 3 trial among mid-adult women and the high and durable efficacy of the 9vHPV vaccine, the FDA approved this change in indication on October 5, 2018, within 6 months of the application submission.<sup>1</sup>

The objectives of this document are:

1. To summarize scientific evidence that MAPs continue to acquire new HPV infections that can progress to high-grade disease and cancer, and
2. To explain health-economic modeling to assess the cost-effectiveness of MAP vaccination, to identify model differences that may impact cost-effectiveness, and to propose steps necessary to ensure alignment. Details regarding this Summary document are provided in the Appendix.

### ***The need for vaccination of 27-45 year olds***

**Only about 15% of MAPs were vaccinated when they were age-eligible for an HPV vaccine as adolescents and young adults.** Approximately 80 million MAPs (27-45 years old) live in the United States. Although approximately 44% of MAPs were age-eligible for HPV vaccination as adolescents and young adults, an estimated 84% to 87% have not been vaccinated.<sup>2</sup>

**MAPs are susceptible to new HPV vaccine-preventable infections.** Adult women can be protected against the 9vHPV vaccine types to which they are naïve. As with young women, most HPV infections in adult women are likely to contain only one HPV type. It is unlikely that women have already been exposed to all 9vHPV vaccine types, which suggests the vaccine can provide protection to the vast majority of MAPs. For example, at baseline in the clinical trial of 4vHPV (V501-019) in adult women (24- to 45 years of age),<sup>3</sup> ~67% of participants from North America had no anogenital HPV infection for any HPV type covered by the 9vHPV vaccine, ~21% had an anogenital infection with at least one 9vHPV

vaccine type, no women tested positive for all 9vHPV vaccine types, and <4% were infected with 3 or more HPV types among the 12 high-risk HPV types assayed. Infections with non-vaccine types (HPV 35/39/51/56/59) were present in 12% of adult women (Merck unpublished data). The HPV infection pattern in adult women is similar to that observed in young women.

**Sexual behavior throughout adulthood puts MAPs at risk for acquisition of new HPV infections.**

Acquiring new sex partners is a primary risk factor for cervical HPV infection, even in women over age 40, and after control for lifetime number of sex partners.<sup>4</sup> In recent national surveys, between 4% and 21% of MAPs reported having 2 or more sex partners in the prior 12 months.<sup>5,6</sup> In the placebo arm of the adult women clinical trial (V501-Protocol 019), women who reported having 1 new sex partner in the 6-month period prior to baseline had twice the risk of developing an incident infection as those who had no new sex partners in the same time period, and women who reported having 2-3 new sex partners in the 6-month period prior to baseline had 3.5 times the risk of developing an incident infection as those who reported having no new sex partners.<sup>3</sup> Some MAP sub-groups are likely to be at particularly high risk of HPV acquisition, including:

- *Previously married and not cohabitating persons:* In the 2002 US National Survey of Family Growth (NSFG),<sup>5</sup> about 9.9% of women and 7.0% of men 15-44 years of age (85% of whom were 30-44 year-olds) were previously married and not cohabitating. Of these, 19.1% of women and 48.6% of men had 15 or more lifetime partners compared with 6.9% and 15.9% of 20- to 24-year-old women and men, respectively.<sup>5</sup>
- *Adult online daters:* Adult women with greater-than-average risk continue to acquire new HPV infections as seen by the incidence of infections in this group.<sup>7</sup>
- *Men who have sex with men (MSM) and men who have sex with men and women (MSMW):* Incidence of anal infection with at least one of the HPV types targeted by 9vHPV vaccine is about 6 times higher among MSM/ MSMW 18-70 years of age when compared to heterosexual men.<sup>8</sup>

**MAPs acquire new HPV infections.** As seen in the placebo arm of the adult women trial of 4vHPV vaccine (Protocol 019), as well as 2vHPV vaccine trials and other observational cohort studies (described herein), adults acquire HPV infection, and a number of these infections persist, thereby increasing the probability of progression to cervical precancers (CIN2+) and cervical cancer. In the placebo arm of the adult woman trial (Protocol 019), over 50% of incident HPV anogenital infections containing any 9vHPV vaccine type progressed to persistent infection. Over 48 months of follow-up, the cumulative risk of

incident and incident persistent infection of  $\geq 6$  months duration with any 9vHPV vaccine type was 19.4% and 10.2%, respectively.<sup>3</sup>

**HPV infections in MAPs can progress to high-grade disease at rates similar to young women.**

- Analyses of the placebo groups of the 4vHPV vaccine efficacy studies in young and mid-adult females show that the rate of progression of HPV16/18-related persistent infection to HPV16/18-related CIN2+ in women 16-26 years of age (2.6/100 person-yrs; 95% CI: 2.0 to 3.3) is similar to that in women 27-45 years of age (2.9/100 person-yrs; 95% CI 1.9 to 4.3).<sup>9</sup> Analyses of the placebo groups of the 4vHPV vaccine efficacy studies in young and mid-adult females show that the rate of progression of HPV16/18-related persistent infection to HPV16/18-related CIN2+ in women 16-26 years of age (2.6/100 person-years; 95% CI: 2.0 to 3.3) is similar to that in women 27-45 years of age (2.9/100 person-years; 95% CI 1.9 to 4.3).<sup>10</sup>
- Similarly, an analysis of the placebo arm of the bivalent HPV (2vHPV) vaccine efficacy study in women older than 25 years of age (~90% of whom were 25-45 years old) demonstrated that high-risk persistent HPV infections lasting  $\geq 6$  months in adult women progress within 48 months to low grade and high-grade cervical lesions at rates similar to young women (~15% and 10%, respectively).<sup>11</sup>
- In the placebo group of a 4vHPV vaccine trial (V501-019)<sup>3</sup> among mid-adult women, 24-45 years of age, 44% of mid-adult women with baseline HPV infection and 18% without baseline HPV infection developed atypical squamous cells of undetermined significance (ASC-US) or worse during the 4 years of follow-up. Approximately 6% and 0.4% of adult women with and without infection with any of 14 measured HPV types at baseline, respectively, developed atypical squamous cells of high significance (ASC-H) or worse.<sup>3</sup>

**Approximately 50% of CIN2+ in the US results from incident HPV infections acquired over the age of 26 years.** Estimates of the burden of CIN2+ caused by high-risk 9vHPV vaccine types acquired during the young adult years, in comparison to the mid-adult years, can be helpful in evaluating the value of vaccinating adult women. We estimated the number of CIN2+ lesions in young and adult women attributable to the 7 high-risk types in the 9vHPV vaccine (Merck unpublished data). In brief, we used type-specific HPV incident infection rates from the placebo groups of the young and adult women clinical trials of 4vHPV vaccine. We applied progression rates to calculate the number of lesions, and we

also back-calculated the number of lesions using published rates of CIN2+. Methods are further described in the attached Appendix.

Our findings suggest:

- Annual number of CIN2+ cases in US caused by any HPV type: **197,444 - 208,645**
- Of these, annual number of CIN2+ cases caused by any of the 7 high-risk types targeted by 9vHPV vaccine: **148,192 – 155,405**, of which:
  - **75,318 – 82,531** arise from infections acquired prior to age 27
  - **72,275 - 72,874** arise from infections acquired at 27 years of age or older

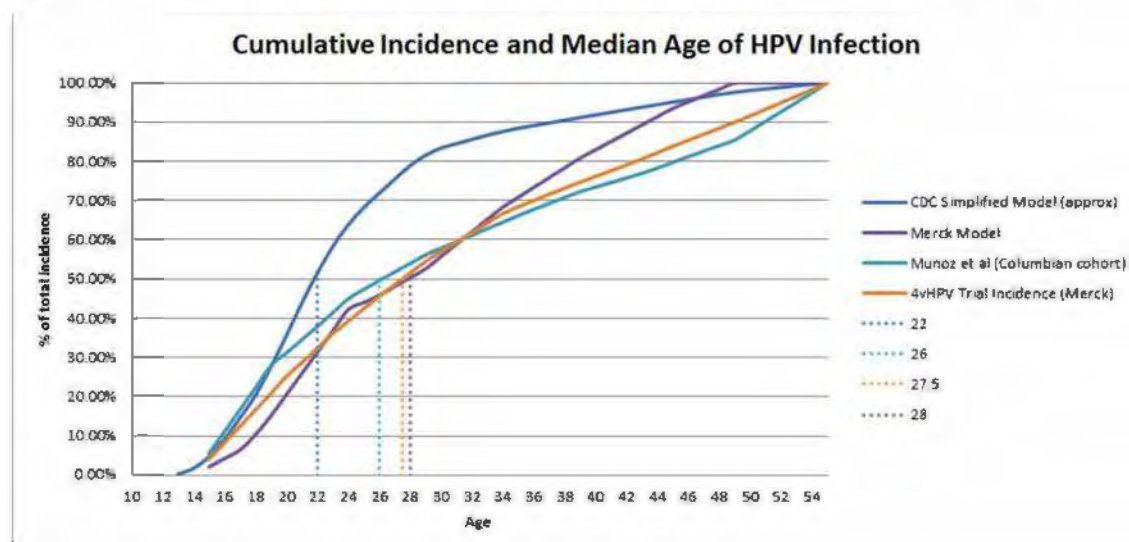
In models used to calculate the number of lesions from rates of HPV infections and probabilities of progression, we estimate that approximately 59,957 CIN2+ cases are caused by persistent infections acquired within the prior 24 months. Approximately 88,048 CIN2+ cases were estimated from incident infections that progress within 12 months, and approximately 130,028 incident infections were estimated to progress to CIN2+ within 36 months. We note that the number of CIN2+ cases using the 12 month progression probabilities (88,048) is quite similar to the annual number of CIN2+ cases noted above for women under 27 years old at the time of their causal HPV infection. Also noteworthy is the consistency between these estimates and the median age at HPV infection acquisition described below.

#### ***Cost-effectiveness evaluation of 9vHPV vaccine in 27-45 year old women and men***

- Cost-effectiveness evaluations of 9vHPV vaccine in 27-45 year olds from three peer-reviewed models will be presented at the October 2018 ACIP meeting: the CDC simplified model<sup>12</sup>, the HPV-ADVISE model<sup>13</sup>, and the Merck model<sup>14</sup>.
- Historically, all 3 model results have yielded similar cost-effectiveness results among younger cohorts during economic evaluations presented at 5 previous ACIP meetings<sup>15,16,17,18,19</sup> and in published meta-analyses.<sup>20,21</sup> However, the cost-effectiveness results of the three models diverge when assessing the economic value of MAP vaccination.
- According to the Merck model, MAP vaccination was cost-effective compared with the current ACIP recommendations for routine vaccination of 9-26 year old females and 9-21 year old males. Results were robust to variations in model structure and many model parameter inputs.

- The CDC simplified model and the HPV-ADVISE model predict that MAP vaccination would not be cost-effective (personal communication).
- The Merck model predicts more clinical (including more HPV-related cancers averted) and economic benefits of MAP vaccination than the CDC simplified model. Some of the possible reasons for different model results are provided in Table 3, with factors driving differences described in greater detail below. Key factors include HPV acquisition rates, clearance of HPV infection, the way partnerships are modeled, and the time to progression of cancer.
- Median age of HPV acquisition: The Merck model predicts a **median age of HPV acquisition of 27 years (Figure 1)**, compared with other model-based estimates such as 21-22 years (approximation) for the CDC simplified model and HPV-ADVISE model, and 20.6 years by Burger et al.<sup>22</sup> (further details available in the Appendix). An estimated lower median age of HPV acquisition results in less benefit of MAP vaccination compared with a higher median age, as fewer unvaccinated persons may be infected during mid-adulthood.
  - The median age of HPV infection acquisition of 27 years is consistent with estimates of annual incidence of HPV infections derived by taking the product of incidence rates from the placebo arm of 4vHPV trials<sup>3</sup>/Colombia cohort,<sup>23</sup> and the 2017 US population in those age cohorts.
  - A median age of approximately 27 years is also supported by sexual behavior data from the 2002 US NSFG<sup>5</sup> which show that MAPs continue to be sexually active. The cumulative risk is comparable as the 27-45 year cohort encompasses 19 years of life, compared with 12 years for 15-26 year-olds.

**Figure 1: Cumulative annual incidence of HPV infection, model vs. derived estimates**



- Clearance of HPV infection and reinfection:
  - The CDC simplified model does not allow for clearance of HPV infection. This absence of clearance in the CDC simplified model reduces infection among MAPs. The Merck model allows for clearance of HPV infection and considers that a proportion of individuals who have cleared their initial HPV infections remain susceptible. This is consistent with the published natural history of HPV infection.<sup>24,25,26</sup> The clearance/reinfection assumptions in the Merck model are more conservative than those reported in a recent meta-analysis by Beachler et al.<sup>27</sup>
- Sexual mixing behavior:
  - Although the HPV-ADVISE model and the Merck model use similar underlying sexual behavior data, the models differ substantially in the way partnerships are modeled. Model-based assumptions regarding partnership formation and ability to mix with older age groups may have resulted in lower levels of sexual partnerships and reduced infection among MAPs in the HPV-ADVISE model, resulting in less benefit from vaccinating MAPs.
- An assumption of longer time to progression to cancer in the HPV-ADVISE model may render fewer benefits to vaccinated MAPs due to the competing risk of other causes of mortality.
- HPV acquisition rates among MAPs in the CDC simplified model, derived from previously published models, are lower than more contemporary and rigorous estimates of incidence rates from clinical trials<sup>3</sup> or population cohort studies.<sup>23</sup>



**Table 3: Potential reasons for differences in model results**

| Variable                                                            | CDC simplified model                                                                                          | HPV-ADVISE model                                                                                                                              | Merck model                                                                                                                                   |
|---------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| Model type                                                          | Simplified transmission dynamic model                                                                         | Individual simulation model                                                                                                                   | Transmission dynamic model                                                                                                                    |
| Predicted median age of HPV infection (years)                       | 22 (approximate)                                                                                              | 22 (approximate)                                                                                                                              | 27                                                                                                                                            |
| Model structure                                                     | Deterministic, compartmental, Susceptible-Infected (SI) model. Persons infected cannot recover from infection | Stochastic, individual-based, Susceptible-Infected-Recovered-Susceptible (SIRS) model. Persons infected can recover and can be infected again | Deterministic, compartmental, Susceptible-Infected-Recovered-Susceptible (SIRS) model. Persons infected can recover and can be infected again |
| Natural immunity                                                    | <i>Not modeled.</i> Assumes infection with HPV 16 provides lifelong natural immunity against HPV 16.          | Assumes probability of developing lifelong natural immunity after clearance of infection based on an uninformed distribution.                 | Assumes seroconversion and natural immunity after infection are based on literature and are consistent with meta-analysis <sup>27</sup> .     |
| HPV infection acquisition                                           | Input to model. HPV acquisition rates for MAP substantially lower than that for younger cohorts               | Determined by the model analysis (Derived within)                                                                                             | Determined by the model analysis (Derived within)                                                                                             |
| Sexual behavior module design                                       | <i>Not applicable</i>                                                                                         | Highly Complex <sup>a</sup>                                                                                                                   | Complex <sup>b</sup>                                                                                                                          |
| Sexual mixing (likelihood of having sex with a person of older age) | <i>Not applicable</i>                                                                                         | Less than US NSFG. Women likely to partner with men of closer age                                                                             | Broader than US NSFG. Women and men likely to partner with opposite gender of wider age range                                                 |
| Duration of progression from CIN3 to cancer for HPV 16              | Transition from HPV acquisition to HPV-associated diseases not modeled                                        | Duration of progression from CIN3 to cancer is Gamma distribution, (range of 25-40 years, all types)                                          | CIN3 progresses to local cancer in 21 years (for HPV 16/18) or 35 years (for HPV 31/33/45/52/58).                                             |
| Costs                                                               | Median costs                                                                                                  | Inputs not available at time of this analysis                                                                                                 | Mean costs                                                                                                                                    |

**Steps necessary for alignment**

- A cross-validation exercise<sup>28</sup> across all 3 models could help assess and resolve the differences in the model results. The proposed details of this exercise can be found in the Appendix.

<sup>a</sup> Level of sexual activity based on number of lifetime partners; Initiation of sexual activity at a rate that depends on age and level of sexual activity; partner acquisition rate which is then attributed to each sexual activity level by age; a stochastic pair formation and separation process, driven by females. Only monogamous stable and casual partnerships are modeled; A mixing matrix that enables females to select a male partner reflecting preferences for age and sexual activity of an individual

<sup>b</sup> Level of sexual activity based on mean number of partners in previous year; a mixing matrix that enables persons to select partner of opposite gender reflecting preferences for age and sexual activity

## ***Conclusions***

- HPV disease is a significant medical concern for MAPs, who continue to acquire new HPV infections that can progress to high-grade disease and cancer.
- Our findings suggest that approximately 50% of CIN2+ cases in the US result from incident HPV infections acquired after the age of 26 years. It is estimated that each year 72,275 - 72,874 cases of CIN2+ attributable to the 7 high risk types in the 9vHPV vaccine arise from infections acquired at age 27 years or older.
- The median age of incident HPV infection of approximately 27 years is also supported by estimates of cumulative HPV infections from the Merck Model, and of annual incident infection obtained from trial/cohort based transmission rates applied to the US population. It is necessary to align the cost-effectiveness modeling on this crucial aspect of HPV infection.
- Sub-groups of MAPs such as persons previously married and not cohabitating, MSM, and MSMW, and online daters are at an even higher risk of acquiring HPV.
- Given that all three models of the cost effectiveness of 9vHPV vaccine in 27-45 year olds have been extensively peer-reviewed and cited, and historically yielded similar cost effectiveness results in younger cohorts, a detailed cross-validation and review of the models is needed to clarify the differences between the models in the MAP population, in order to help decision makers accurately assess the true economic value of HPV vaccination in this age group.

## References

- <sup>1</sup> Gardasil 9 Prescribing Information
- <sup>2</sup> Estimates from Merck Model using NHANES and NIS-TEEN data (details in Appendix)
- <sup>3</sup> Merck & Co., Inc. Data on file
- <sup>4</sup> Trottier H, Ferreira S, Thomann P, Costa MC, Sobrinho JS, Prado JC, et al. Human papillomavirus infection and reinfection in adult women: the role of sexual activity and natural immunity. *Cancer Res.* 2010 Nov 1;70(21):8569-77
- <sup>5</sup> Mosher WD., Chandra A., Jones J. Sexual behavior and selected health measures: men and women 15-44 years of age, United States, 2002. *Advance data.* 2005(362):1-55.
- <sup>6</sup> Chandra A., Mosher WD, Copen C, Sionean C. Sexual behavior, sexual attraction, and sexual identity in the United States: data from the 2006-2008 National Survey of Family Growth, 2011 Mar 3;(36):1-36
- <sup>7</sup> Winer RL, Hughes JP, JE, Xi LF, Koutsky LA. Incident detection of high-risk Human Papillomavirus infections in a cohort of high-risk women aged 25-65 Years. *J Infect Dis.* 2016 Sep 1;214(5):665-75
- <sup>8</sup> Sudenga SL, Nyitray AG, Torres BN, Silva R, Villa L, Lazzcano-Ponce E, et al. Comparison of anal HPV natural history among men by country of residence: Brazil, Mexico, and the United States. *J Infect.* 2017 Mar 28. [Epub ahead of print].
- <sup>9</sup> Bautista O, Saah A, Munoz N. Longitudinal study of human papillomavirus persistence and cervical intraepithelial neoplasia grade 2/3: critical role of duration of infection. *J Natl Cancer Inst* 2011; 103:158.
- <sup>10</sup> Bautista O, Saah A, Munoz N. Longitudinal study of human papillomavirus persistence and cervical intraepithelial neoplasia grade 2/3: critical role of duration of infection. *J Natl Cancer Inst* 2011; 103:158.
- <sup>11</sup> Skinner SR, Wheeler CM, Romanowski B, et al; VIVIANE Study Group. Progression of HPV infection to detectable cervical lesions or clearance in adult women: Analysis of the control arm of the VIVIANE study. *Int J Cancer.* 2016;138(10):2428-38
- <sup>12</sup> Chesson HW, Markowitz LE, Hariri S, Ekwueme DU, Saraiya M. The impact and cost-effectiveness of nonavalent HPV vaccination in the United States: Estimates from a simplified transmission model, 2016 Jun 2; 12(6):1363-72.
- <sup>13</sup> Brisson M., Laprise JM, Chesson HW, Drolet M., Malagon T., Boily MC, Markowitz LE. Health and Economic Impact of Switching from a 4-Valent to a 9-Valent HPV Vaccination Program in the United States, 2015 Oct 4; 108(1). pii: djv282
- <sup>14</sup> Elbasha EH, Dasbach J. Impact of vaccinating boys and men against HPV in the United States. *Vaccine.* 2010;28(42):6858-67
- <sup>15</sup> <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-feb08-508.pdf>, accessed 10/18/2018
- <sup>16</sup> <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-oct10.pdf>, accessed 10/18/2018
- <sup>17</sup> <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-feb11.pdf>, accessed 10/18/2018
- <sup>18</sup> <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-2015-02.pdf>, accessed 10/18/2018
- <sup>19</sup> <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-2015-06.pdf>, accessed 10/18/2018
- <sup>20</sup> Brisson M., Bénard É., Drolet M. et al. Population-level impact, herd immunity, and elimination after human papillomavirus vaccination: a systematic review and meta-analysis of predictions from transmission-dynamic models. *The Lancet Public Health.* 2016;1.
- <sup>21</sup> Jit M., Demarteau N., Elbasha E. et al. Human papillomavirus vaccine introduction in low-income and middle-income countries: guidance on the use of cost-effectiveness models. *BMC Med.* 2011 May 12; 9:54.
- <sup>22</sup> Burger, et al Age of Acquiring Causal Human Papillomavirus (HPV) Infections: Leveraging Simulation Models to Explore the Natural History of HPV-induced Cervical Cancer. *Clinical Infectious Diseases®* 2017;65(6):893-9
- <sup>23</sup> Munoz N., Mendez F., et al. 2004. Incidence, Duration, and Determinants of Cervical Human Papillomavirus Infection in a Cohort of Colombian Women with Normal Cytological Results. *JID.* 2004:190
- <sup>24</sup> Trottier H, Ferreira S, Thomann P, Costa MC, Sobrinho JS, Prado JC, et al. Human papillomavirus infection and reinfection in adult women: the role of sexual activity and natural immunity. *Cancer Res.* 2010 Nov 1;70(21):8569-77
- <sup>25</sup> Velicer C, Zhu X, Vuocolo S, Liaw K, Saah A. 2009. Prevalence and Incidence of HPV Genital Infection in Women. *Sexually Transmitted Diseases: November 2009 - Volume 36 - Issue 11 - p 696-703*
- <sup>26</sup> Fu TC, Carter JJ, Hughes JP, Feng Q, Hawes SE, Schwartz SM, et al. Re-detection vs. new acquisition of high-risk human papillomavirus in mid-adult women. *Int J Cancer* 2016; 139(10):2201-12.
- <sup>27</sup> Beachler DC, Jenkins G, Safaeian M, Kreimer AR, Wentzensen N. Beach. Natural Acquired Immunity Against Subsequent Genital Human Papillomavirus Infection: A Systematic Review and Meta-analysis. *J Infect Dis.* 2016 May 1; 213(9):1444-54.
- <sup>28</sup> Eddy D, Hollingworth W, Caro J, Tsevat J, McDonald K, Wong J, On Behalf of the ISPOR-SMDM Modeling Good Research Practices Task Force. Model Transparency and Validation. 2012. A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force 7. *Medical Decision making, Sep.-Oct. 2013.* DOI: 10.1177/0272989X12454579

***Appendix***

**The Need for HPV Vaccination in Mid-Adult Persons 27-45 Years Old  
and  
Differences in Cost-effectiveness Models**

**Merck & Co., Inc.**

**October 22, 2018**

## **Table of Contents**

|       |                                                                                           |    |
|-------|-------------------------------------------------------------------------------------------|----|
| 1     | Background                                                                                | 5  |
| 2     | The need for MAP vaccination                                                              | 5  |
| 2.1   | Most MAPs are unvaccinated                                                                | 5  |
| 2.2   | A substantial number of mid-adults have behaviors that put them at risk for HPV infection | 5  |
| 2.3   | MAPs include sub-groups at high risk of HPV acquisition.                                  | 9  |
| 2.3.1 | Previously married and not cohabitating individuals                                       | 10 |
| 2.3.2 | Married women in their first marriage vs. other women                                     | 11 |
| 2.3.3 | MSM and MSMW                                                                              | 11 |
| 2.4   | Mid-adults are susceptible to new HPV infections                                          | 11 |
| 2.5   | Mid-adults can acquire new HPV infections                                                 | 11 |
| 2.6   | Acquiring new sex partners is a risk factor of HPV infection                              | 12 |
| 2.7   | Adult men also acquire HPV infections                                                     | 12 |
| 2.8   | US adults acquire new HPV infections which can progress to HPV-related disease            | 12 |
| 2.9   | Estimates of CIN2+ in Young Women and Adult Women in the United States                    | 14 |
| 2.9.1 | Details of CIN2+ Lesion Analysis                                                          | 15 |
| 3     | Cost-effectiveness analysis of 9vHPV in 27-45 year olds                                   | 20 |
| 3.1   | Cost-effectiveness results                                                                | 21 |
| 3.2   | Median age of HPV infection                                                               | 22 |
| 3.3   | History of convergence of cost-effectiveness models for younger cohorts                   | 23 |
| 4     | Differences in models                                                                     | 24 |
| 4.1   | Model structure                                                                           | 24 |
| 4.2   | HPV acquisition/ transmission                                                             | 26 |
| 4.2.1 | HPV-acquisition in the CDC simplified model                                               | 26 |
| 4.2.2 | HPV-acquisition in the HPV-ADVISE model                                                   | 26 |
| 4.2.3 | HPV-acquisition in the Merck model                                                        | 28 |
| 4.2.4 | Summary of HPV-acquisition/transmission across the 3 models                               | 28 |
| 4.3   | Duration of progression from CIN3 to cervical cancer                                      | 28 |
| 4.4   | Other minor differences                                                                   | 28 |
| 5     | Cross-validation                                                                          | 29 |
| 6     | Conclusions                                                                               | 29 |
| 7     | References                                                                                | 30 |

## List of Figures

|                                                                                                                                                                                                                                                        |    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Figure 1: Prevalence of HPV Anogenital infection (Day 1) in 4vHPV clinical trials                                                                                                                                                                      | 11 |
| Figure 2: Risk of detecting a CIN1+ or CIN2+ associated with the same HPV type for 6-month persistent infections in placebo groups: comparison of women over 25 years of age versus women 15 to 25 years of age – VIVIANE and PATRICIA trials of 2vHPV | 13 |
| Figure 3: Cumulative incidence of ASC-H/HSIL or worse Pap outcomes (by Day 1 HPV infection status) among adult women in Protocol 019                                                                                                                   | 14 |
| Figure 4: Cumulative annual incidence of HPV infection                                                                                                                                                                                                 | 23 |
| Figure 5: Partner acquisition rates of sexually active males in the HPV-ADVISE model                                                                                                                                                                   | 27 |

## List of Tables

|                                                                                                                                                                                                                         |    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Table 1: Distribution of number of partners in the previous year, by age and gender, 2006-2008                                                                                                                          | 6  |
| Table 2: Number of opposite-sex partners in lifetime for men and women 15-44 years of age, (2002)                                                                                                                       | 8  |
| Table 3: Median Number of Lifetime Sex Partners (LTSP)                                                                                                                                                                  | 8  |
| Table 4: Number of Sex Partners In Prior 12 Months Among US Adults, 21-40 Years Old                                                                                                                                     | 9  |
| Table 5: Sexual behavior of persons previously married and not cohabitating: United States, 2002                                                                                                                        | 10 |
| Table 6: Annual Number of CIN2+ Lesions in the United States Attributed to 9vHPV Vaccine High-Risk HPV Types: Estimated from Rates of CIN2+ and Proportional Attribution of HPV Types in Lesions                        | 14 |
| Table 7: Annual Number of CIN2+ Lesions Attributed to 9vHPV Vaccine High Risk HPV Types in the United States: Diagnosed in Women 21-29 Years Old with Causal Infection Starting Before Age 27 (Merck, unpublished data) | 15 |
| Table 8: Rates of CIN2+ Used to Estimate Annual Number of CIN2+ Cases in the US                                                                                                                                         | 16 |
| Table 9: Rates and Variables Used to Estimate Annual Number of CIN2+ Lesions in United States                                                                                                                           | 18 |
| Table 10: Rates and Variables Used to Estimate Annual Number of CIN2+ Lesions in United States                                                                                                                          | 18 |
| Table 11: Rates and Variables Used to Estimate Annual Number of CIN2+ Lesions in United States                                                                                                                          | 18 |
| Table 12: Annual Number of CIN2+ Lesions Attributed to HPV 16/18/31/33/45/52/58 in the United States Diagnosed in Women 21-29 Years Old                                                                                 | 19 |
| Table 13: Annual Number of CIN2+ Lesions Attributed to HPV 16/18/31/33/45/52/58 in the United States Diagnosed in Women 21-29 Years Old                                                                                 | 20 |
| Table 14: Comparison of CDC simplified model and Merck model (using similar assumptions)                                                                                                                                | 22 |
| Table 15: Incidence rates of High-Risk HPV (any type) among women from 4vHPV clinical trials and Columbian cohort                                                                                                       | 23 |
| Table 16: Parameters of natural history of HPV disease                                                                                                                                                                  | 25 |
| Table 17: Efficacy against HPV6/11/16/18-related persistent infection and disease in seropositive and PCR-negative subjects in clinical trials of 4vHPV vs placebo                                                      | 25 |

## Abbreviations

| Abbreviation | Description                                       |
|--------------|---------------------------------------------------|
| ACIP         | Advisory Committee on Immunization Practices      |
| CDC          | Centers for Disease Control and Prevention        |
| CI           | Confidence interval                               |
| CIN          | Cervical Intraepithelial Neoplasia                |
| FDA          | Food and Drug Administration Of The United States |
| HPV          | Human Papillomavirus                              |
| HR           | High Risk                                         |
| ICER         | Incremental Cost-Effectiveness Ratio              |
| MAP          | Mid-adult person                                  |
| NCHS         | National Center for Health Statistics             |
| NIS-Teen     | National Immunization Survey - Teenagers          |
| NHANES       | National Health and Nutrition Examination Survey  |
| NSFG         | National Survey of Family Growth                  |
| QALY         | Quality-Adjusted Life Year                        |
| US           | United States                                     |
| 9vHPV        | Nonavalent HPV vaccine                            |



# 1 Background

Based on a significant unmet medical need for protection against HPV among mid-adult persons (MAPs) 27 through 45 years of age, the FDA recently granted priority review for Merck's application to extend the upper age indication of the nine-valent human papillomavirus (9vHPV) vaccine from 26 to 45 years. Based on the strong evidence provided in the application, including a substantial event rate for HPV disease among placebo-recipients in the Phase 3 trial among mid-adult women and the high and durable efficacy of the 9vHPV vaccine, the FDA approved this change in indication on October 5, 2018, within 6 months of the application submission.<sup>1</sup> Cost-effectiveness analysis to evaluate vaccination of MAPs from three peer-reviewed models—the CDC simplified model<sup>2</sup>, the HPV-ADVISE model<sup>3</sup>, and the Merck model<sup>4</sup>--will be presented at the October 2018 ACIP meeting.

The objective of this Appendix is to provide detailed scientific information regarding the facts presented in the accompanying Summary document.

## 2 The need for MAP vaccination

### 2.1 *Most MAPs are unvaccinated*

Approximately 80 million MAPs (27 to 45 years old) live in the United States (US). Millions are sexually active and at risk for acquiring HPV.

We used the Merck model vaccination coverage to estimate the number of 27 to 45 year old women and 20-45 year old men in the vaccinated population.

- We estimated the number of people in this cohort and the number of people who were age-eligible (females 15-26 in 2007, men 13-21 in 2011) from this cohort at the beginning of 2019.
- We then estimated the number of people who had been given at least one dose of HPV vaccine in this age cohort by the end of 2018 using National Health and Nutrition Examination Survey (NHANES)<sup>5</sup> and National Immunization Survey–Teen (NIS-Teen)<sup>6</sup> coverage estimates.
- Of the approximately 44% of those MAPs who were age-eligible for HPV vaccination, an estimated 84%-87% have not been vaccinated.

Individuals in this age range continue to be susceptible to HPV infections that can be prevented by use of the 9vHPV vaccine.

### 2.2 *A substantial number of mid-adults have behaviors that put them at risk for HPV infection*

Understanding sexual behavior in the US population is important so that transmission dynamics are accurately captured for disease burden estimates and cost effectiveness models.

Sexual behavior in the US is reported through several national surveys. One of these surveys is the National Survey of Family Growth (NSFG), which is conducted by the Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics (NCHS) among males and females 15 to 44 years of age in the United States. It is based on in-person, face-to-face interviews. In the NSFG<sup>7, 8</sup>:

- Between 4% and 21% of MAPs reported having 2 or more sex partners in the prior 12 months. Number of recent sex partners is a strong risk factor for HPV infection acquisition (Table 1).

**Table 1: Distribution of number of partners in the previous year, by age and gender, 2006-2008**

| Age group (years) | Number of opposite-sex sexual partners in last 12 months (among females) |       |       |      |      | Average <sup>‡</sup> # of Partners | Number of opposite-sex sexual partners in last 12 months (among males) |       |       |      |      | Average <sup>‡</sup> # of Partners |
|-------------------|--------------------------------------------------------------------------|-------|-------|------|------|------------------------------------|------------------------------------------------------------------------|-------|-------|------|------|------------------------------------|
|                   | 0                                                                        | 1     | 2     | 3    | 4+   |                                    | 0                                                                      | 1     | 2     | 3    | 4+   |                                    |
| <b>15-19</b>      | 52.7%                                                                    | 27.7% | 9.8%  | 3.4% | 5.3% | 1.1                                | 49.8%                                                                  | 25.6% | 11.1% | 5.0% | 5.6% | 1.2                                |
| <b>20-24</b>      | 17.0%                                                                    | 57.8% | 14.1% | 5.1% | 4.6% | 1.5                                | 20.2%                                                                  | 49.8% | 12.2% | 6.8% | 9.5% | 1.9                                |
| <b>25-29</b>      | 9.0%                                                                     | 75.8% | 8.2%  | 3.6% | 2.7% | 1.3                                | 9.4%                                                                   | 68.6% | 9.7%  | 4.0% | 7.5% | 1.8                                |
| <b>30-34</b>      | 6.5%                                                                     | 82.8% | 5.5%  | 1.7% | 2.9% | 1.3                                | 7.9%                                                                   | 77.4% | 6.2%  | 2.4% | 5.1% | 1.5                                |
| <b>35-39</b>      | 7.6%                                                                     | 86.2% | 4.3%  | 0.9% | 0.7% | 1.0                                | 7.0%                                                                   | 77.2% | 7.3%  | 3.4% | 4.4% | 1.5                                |
| <b>40-44</b>      | 9.4%                                                                     | 84.2% | 3.9%  | 0.6% | 1.2% | 1.1                                | 10.3%                                                                  | 78.6% | 4.7%  | 1.7% | 3.6% | 1.3                                |

<sup>‡</sup> Average number of sexual partners was estimated assuming persons with 4+ partners had a mean of 10 partners.

Source: Chandra 2011 (US NSFG 2006-2008)<sup>8</sup>

- The average number of sexual partners in the previous 12 months has remained steady among all age groups ranging from 1.0 to 1.5 partners per year for various 5-year age groups of women, and 1.2 to 1.9 partners for men (Table 1).
- Data on lifetime partners from the 2002 NSFG survey<sup>9</sup> showed a similar trend as the 2006-2008 survey (

- Table 2).
- The median number of lifetime partners increased during mid-adulthood: 25- to 44-year-old men reported a median of 6.7 partners, compared to 3.8 among young men aged 20 to 24 years; among women, 25- to 44-year-olds reported a median of 3.8 lifetime partners, compared to 2.8 among 20- to 24-year-olds (Table 2).
- Having had 15 or more lifetime partners was reported by approximately 11% to 12% of adult women, and 24% to 34% of adult males, compared to 6.9% and 15.9% of 20- to 24-year-old women and men, respectively.

The National Health and Nutrition Examination Surveys (NHANES) also report sexual behavior data in a nationally representative sample of the non-institutionalized US population. Findings of data analyzed for years 1999-2012 indicate:

- The median number of lifetime sexual partners has increased in more recent birth cohorts<sup>10</sup> (Table 3).
- Overall, this implies that new partners continue to be acquired during mid adulthood (i.e., age 25 to 44 years), although a slower rate than during the ages 20 to 24 years (Table 3).
- As noted by Liu et al. 2015, these data also support the notion that risk of HPV infection is greater among birth cohorts who became sexually active after the sexual revolution.

**Table 2: Number of opposite-sex partners in lifetime for men and women 15-44 years of age, (2002)<sup>11</sup>**

| Characteristic           | Number in thousands | Number of opposite sex partners in lifetime |      |      |      |      |      |            |               |
|--------------------------|---------------------|---------------------------------------------|------|------|------|------|------|------------|---------------|
|                          |                     | Total                                       | 0    | 1    | 2    | 3-6  | 7-14 | 15 or more | Median number |
| Percent distribution     |                     |                                             |      |      |      |      |      |            |               |
| Women                    |                     |                                             |      |      |      |      |      |            |               |
| Women 15-44 years of age | 61,561              | 100                                         | 8.6  | 22.5 | 10.8 | 32.6 | 16.3 | 9.2        | 3.3           |
| Age                      |                     |                                             |      |      |      |      |      |            |               |
| 15-19 years              | 9,834               | 100                                         | 37.8 | 27.2 | 9.0  | 19.1 | 5.0  | 1.9        | 1.4           |
| 20-24 years              | 9,840               | 100                                         | 8.9  | 24.6 | 13.0 | 32.2 | 14.4 | 6.9        | 2.8           |
| 25-29 years              | 9,249               | 100                                         | 2.5  | 22.5 | 11.7 | 31.3 | 20.1 | 11.9       | 3.5           |
| 30-34 years              | 10,272              | 100                                         | 1.9  | 20.5 | 9.4  | 38.8 | 18.0 | 11.3       | 3.8           |
| 35-39 years              | 10,853              | 100                                         | 1.1  | 20.2 | 11.2 | 35.8 | 20.5 | 11.2       | 3.8           |
| 40-44 years              | 11,512              | 100                                         | 1.4  | 20.4 | 10.5 | 37.4 | 19.1 | 11.2       | 3.8           |
| Men                      |                     |                                             |      |      |      |      |      |            |               |
| Men 15-44 years of age   | 61,147              | 100                                         | 9.7  | 12.8 | 8.1  | 27.5 | 19.3 | 22.6       | 5.4           |
| Age                      |                     |                                             |      |      |      |      |      |            |               |
| 15-19 years              | 10,208              | 100                                         | 38.5 | 23.0 | 9.2  | 20.7 | 6.2  | 2.5        | 1.9           |
| 20-24 years              | 9,883               | 100                                         | 9.0  | 15.9 | 11.7 | 33.5 | 14.1 | 15.9       | 3.8           |
| 25-44 years              | 41,056              | 100                                         | 2.8  | 9.6  | 7.0  | 27.8 | 23.7 | 29.2       | 6.7           |
| 25-29 years              | 9,226               | 100                                         | 4.9  | 10.0 | 8.8  | 29.4 | 23.2 | 23.8       | 5.9           |
| 30-34 years              | 10,138              | 100                                         | 2.8  | 10.7 | 6.9  | 28.5 | 21.9 | 29.2       | 6.4           |
| 35-39 years              | 10,557              | 100                                         | 2.0  | 8.9  | 7.0  | 28.0 | 25.5 | 28.8       | 6.9           |
| 40-44 years              | 11,135              | 100                                         | 1.9  | 8.8  | 5.4  | 25.6 | 24.2 | 34.2       | 8.2           |

**Table 3: Median Number of Lifetime Sex Partners (LTSP)<sup>12</sup>**

| Birth Cohort | Age (as of 2012) | Females Median LTSP | Males Median LTSP |
|--------------|------------------|---------------------|-------------------|
| 1940-1949    | 63-72            | 2.6                 | 6.7               |
| 1950-1959    | 53-62            | 3.8                 | 7.9               |
| 1960-1969    | 43-52            | 4.5                 | 8.9               |
| 1970-1979    | 33-42            | 5.3                 | 8.8               |
| 1980-1989    | 23-32            | N/A                 | N/A               |

Source: NHANES 1999-2012

Another national survey, the “Monitoring the Future” survey, found results fairly similar to NSFG and NHANES. This survey reported that ≥10% of sexually active females 21-40 years old had more than 1 partner in the prior 12 months (Table 4) (Johnston 2017).<sup>13</sup>

In an analysis of 21-44 year old women in 2006-2010 who reported having at least 1 male sex partner in the prior year (National Survey of Family Growth; Nield et al. 2014)<sup>14</sup>:

- 10% had more than 1 partner (6% concurrent and 4% non-overlapping partnerships)
- Gaps between partners were typically less than 6 months in those with non-overlapping partnerships
- 93% of women in concurrent partnerships and 79% in non-overlapping partnerships had 5 or more lifetime sex partners
- Marriage/cohabitation was not a guarantee of lower risk; 19% of women in concurrent partnerships and 15.5% in non-overlapping partnerships were married or cohabitating.

**Table 4: Number of Sex Partners In Prior 12 Months Among US Adults, 21-40 Years Old**

| Age (Years Data Collected)  | Number of sex partners in last 12 months among those who reported at least one partner (%) |      |      |     |         |          |       |
|-----------------------------|--------------------------------------------------------------------------------------------|------|------|-----|---------|----------|-------|
|                             | 1                                                                                          | 2    | 3    | 4   | 5 to 10 | 11 to 20 | 21+   |
| <b>Heterosexual Females</b> |                                                                                            |      |      |     |         |          |       |
| 21-30 (2004-2016)           | 76.2                                                                                       | 11.3 | 5.7  | 3.6 | 2.8     | 0.3      | 0.1   |
| 35 (2008-2016)              | 89.7                                                                                       | 5.4  | 2.4  | 1.1 | 1.1     | 0.2      | 0.1   |
| 40 (2010-2016)              | 90.9                                                                                       | 5.3  | 2.0  | 0.9 | 0.7     | 0.2      | <0.05 |
| <b>Heterosexual Males</b>   |                                                                                            |      |      |     |         |          |       |
| 21-30 (2004-2016)           | 69.3                                                                                       | 11.1 | 7.0  | 4.6 | 6.3     | 1.1      | 0.6   |
| 35 (2008-2016)              | 86.8                                                                                       | 5.1  | 2.9  | 2.4 | 1.9     | 0.5      | 0.4   |
| 40 (2010-2016)              | 87.8                                                                                       | 4.6  | 3.2  | 1.1 | 2.0     | 0.6      | 0.4   |
| <b>MSM</b>                  |                                                                                            |      |      |     |         |          |       |
| 21-30 (2004-2016)           | 47.8                                                                                       | 12.3 | 10.5 | 8.6 | 11.1    | 5.5      | 4     |
| 35 (2008-2016)              | 46.7                                                                                       | 4.3  | 8.8  | 7.8 | 23.7    | 4.1      | 4.6   |
| 40 (2010-2016)              | 50.8                                                                                       | 13.6 | 8.3  | 4.7 | 15.0    | 2.0      | 5.6   |

Source: (Monitoring the Future National Survey, Johnston 2017<sup>15</sup>)

### **Sexual mixing among MAPs and young adults**

- Data on number of sexual partners in the previous year and number of lifetime sexual partners suggest that women are likely to have older sexual partners.
- Data from the 1995 National Survey of Family Growth (NSFG)<sup>16</sup> show that 9.3%, 17.1%, 17.4%, 21.9%, 19.2%, and 16.2% of 15-19, 20-24, 25-29, 30-34, 35-39, and 40-44 year old women have a male partner who is at least 6 years older.

### **2.3 MAPs include sub-groups at high risk of HPV acquisition.**

Several groups of mid-adults are at high risk of HPV acquisition, including those who are previously married and not cohabitating, and men who have sex with men (MSM), and men who have sex with men and women (MSMW).

### 2.3.1 Previously married and not cohabitating individuals

- Data from the 2002 NSFG study in MAPs reported about 9.9% of women and 7.0% of men age 15–44 years were previously married and not cohabitating. Most (85.0%) of these persons were 30–44 years-old, implying that about 9.4 million persons in the US are previously married and not cohabitating are 30–44 years of age. These persons reported greater sexual activity than even 20–24-year-olds (Table 5).
- The median numbers of lifetime partners reported by women and men who were formerly married and not cohabitating were 5.6 and 11.9, respectively, compared with 2.8 and 3.8 median lifetime opposite sex partners reported by 20- to 24-year-old women, and men, respectively.
- 19.1% of women and 48.6% of men who were formerly married and not cohabitating had 15 or more lifetime partners, compared with 6.9% and 15.9% of 20- to 24-year-old men and women (compare Tables 3 and 4).
- Furthermore, a higher proportion of previously married and not cohabitating women and men reported three or more partners in the previous year compared to 20- to 24-year-olds, the age group that has the highest partner acquisition rate (women: 12.7% vs 9.7%; men: 17.7% vs. 16.3%, Tables 2 and 4).
- These comparisons of sexual activity indicate that MAPs who are formerly married and not cohabitating may be at a higher risk of acquiring HPV than 20- to 24-year-olds.
- The high-risk groups identified by ACIP among those aged 9 to 26 years, such as MSM, are also likely to benefit from the HPV vaccine.

**Table 5: Sexual behavior of persons previously married and not cohabitating: United States, 2002<sup>17</sup>**

| Characteristics                                                                                 | Number in thousands | Number of opposite sex partners |                      |      |      |                  |      |            |               |
|-------------------------------------------------------------------------------------------------|---------------------|---------------------------------|----------------------|------|------|------------------|------|------------|---------------|
|                                                                                                 |                     | Total                           | 0                    | 1    | 2    | 3-6              | 7-14 | 15 or more | Median number |
|                                                                                                 |                     |                                 | Percent distribution |      |      |                  |      |            |               |
| Number of partners in previous year for women who were previously married, and not cohabitating |                     |                                 | -                    | 47.5 | 16.6 | 12.7 (3 or more) |      |            | -             |
| Number of lifetime partners for women who were previously married, and not cohabitating         | 6,096               | 100                             | -                    | 6.5  | 8.1  | 37.8             | 28.5 | 19.1       | 5.6           |
| Number of partners in previous year for men who were previously married, and not cohabitating   |                     |                                 | -                    | 50.1 | 15.9 | 17.7 (3 or more) |      |            |               |
| Number of lifetime partners for men who were previously married, and not cohabitating           | 4,174               | 100                             | -                    | 0.7  | 3.6  | 22.5             | 24.6 | 48.6       | 11.9          |

### 2.3.2 Married women in their first marriage vs. other women

In Protocol V501-019, after adjusting for age, in comparison to women who were married and in their first marriage, all other people in the trial had 50% higher risk of developing an incident infection with at least one of the 7 high risk 9vHPV types.<sup>18</sup>

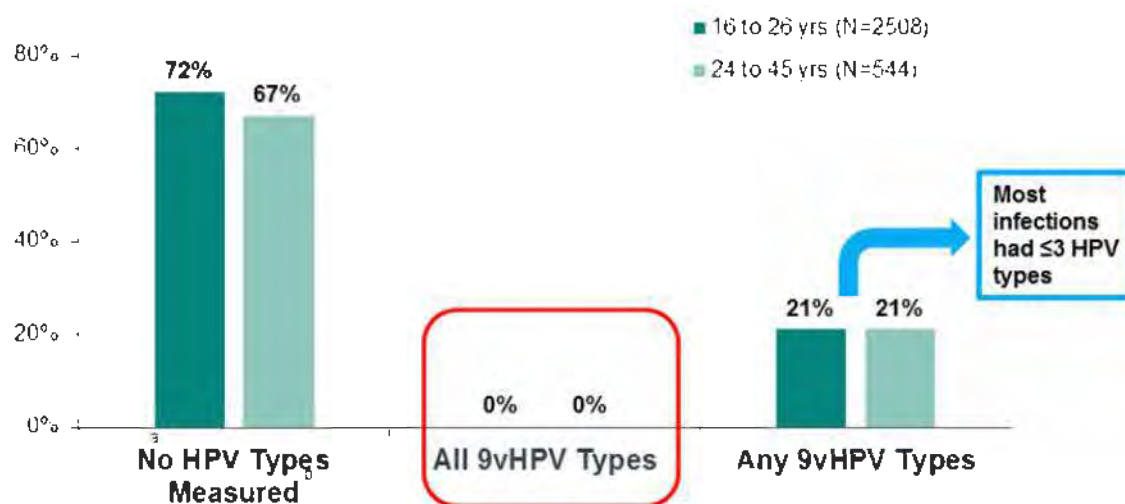
### 2.3.3 MSM and MSMW

Other high-risk groups include men who have sex with men (MSM) and men who have sex with men and women (MSMW). Incidence of anal infection with at least one of the HPV types targeted by 9vHPV was about 6 times higher among men who have sex with men or men who have sex with men and women, compared to heterosexual men.<sup>19</sup>

## 2.4 Mid-adults are susceptible to new HPV infections

Both infected and uninfected adult women are susceptible to new HPV infections, as most HPV infections in adult women are likely to contain only one HPV type and very few have more than 3 HPV types. In the clinical trials of 4vHPV (Protocol V501-013/15 and V501-019) in young and adult women up to 45 years of age,<sup>18</sup> ~ 70% of participants were free from anogenital HPV infection with all 14 HPV types in the Merck PCR assay (Figure 1). No women tested positive for all 9 types in the 9vHPV at baseline, and approximately 21% had an anogenital infection with at least 1 HPV type targeted by the 9vHPV vaccine.

**Figure 1: Prevalence of HPV Anogenital infection (Day 1) in 4vHPV clinical trials**



## 2.5 Mid-adults can acquire new HPV infections

In a 2016 publication evaluating HPV infections in US women 25 to 65 years of age who were online daters,<sup>20</sup> the 12-month incidence of high-risk HPV in vaginal swabs was 25.4% (95% CI: 21.3, 30.1). The study investigators estimated that 64% of the incident high-risk HPV infections in their study were likely new acquisition, whereas about one-third were likely redetections of prior infection.



## ***2.6 Acquiring new sex partners is a risk factor of HPV infection***

Acquiring new sex partners, not age, has been shown to be a primary risk factor for cervical HPV infection in women over age 40<sup>21</sup>.

## ***2.7 Adult men also acquire HPV infections***

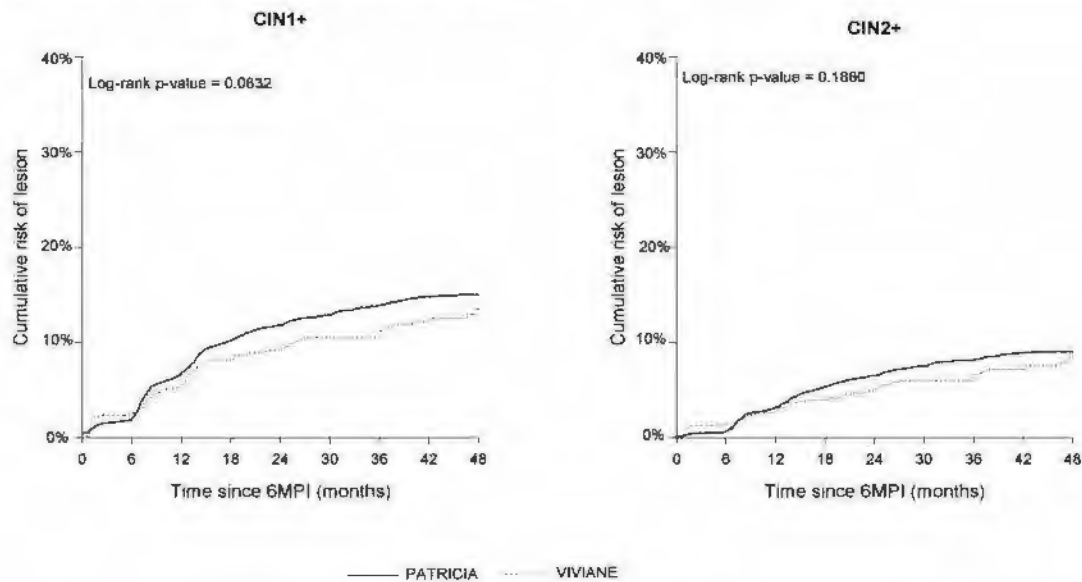
Anal HPV infection is constant across ages in US males. In a sample of 634 males from Tampa, Florida participating in the HPV in Men (HIM) Study<sup>22</sup>, anal infection prevalence did not significantly differ across the groups 18 to 30, 31 to 44, and 45 to 70 years of age (12.6%, 19.4%, 16.2%). The overall HPV prevalence was 15.0% in the entire cohort and 10.2% among men who had sex exclusively with women (MSW). The prevalence with any 9vHPV types was 8.8% in the entire cohort and 6% among MSW.

## ***2.8 US adults acquire new HPV infections which can progress to HPV-related disease***

HPV infections in adults can progress to disease. Merck's trial data demonstrate that young and adult women with an incident HPV infection have similar rates of progression to CIN. Analyses of the placebo groups of the 4vHPV vaccine efficacy studies in young and mid-adult females show that the rate of progression of HPV16/18-related persistent infection to HPV16/18-related CIN2+ in women 16-26 years of age (2.6/100 person-yr; 95% CI:2.0 to 3.3) is similar to that in women 27-45 years of age (2.9/100 person-yr; 95% CI 1.9 to 4.3) with no statistically significant difference.<sup>23</sup>

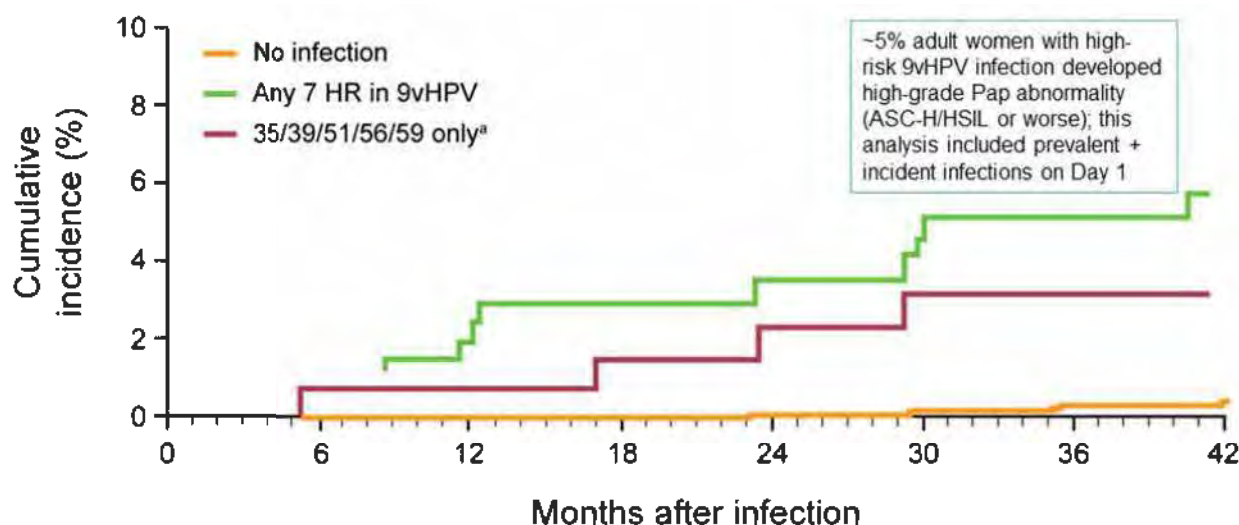
Similarly, data from the 2vHPV vaccine clinical trial (VIVIANE) in adult women >25 years of age (~90% who were 45 years of age or younger) and the PATRICIA trial in women 15-25 years of age demonstrated that rates of progression to low and high grade cervical lesions are similar in young and adult women (Figure 2).<sup>24</sup> High-risk persistent HPV infections lasting ≥6 months in adult women progressed within 48 months to low grade and high-grade cervical lesions (CIN1+ and CIN2+) at rates similar to young women (approximately 15% and 10%, respectively).<sup>24</sup>

**Figure 2: Risk of detecting a CIN1+ or CIN2+ associated with the same HPV type for 6-month persistent infections in placebo groups: comparison of women over 25 years of age versus women 15 to 25 years of age – VIVIANE and PATRICIA trials of 2vHPV**



In addition, Merck's unpublished analyses of adult women (24-45 years of age) in the placebo group of Protocol 019 demonstrate that adult women with HPV infection can develop low and high-grade Pap test abnormalities. Approximately 18% of mid-adult women without baseline HPV infection and 44% with infection developed atypical squamous cells of undetermined significance (ASC-U5) or worse during the 4 years of follow-up. In addition, as shown in Figure 3, approximately 0.4% of adult women with no HPV detected at baseline and 6% of adult women with detection of any of 14 measured HPV types developed ASC-H/HSIL or worse.

**Figure 3: Cumulative incidence of ASC-H/HSIL or worse Pap outcomes (by Day 1 HPV infection status) among adult women in Protocol 019**



ASC-H/HSIL atypical squamous cells cannot rule out HSIL, HSIL high-grade squamous intraepithelial lesion

<sup>a</sup>Non-vaccine types

## 2.9 Estimates of CIN2+ in Young Women and Adult Women in the United States

Estimates of the burden of CIN2+ caused by high-risk 9vHPV vaccine types acquired during the young adult years, in comparison to the mid-adult years, can be helpful in evaluating the value of vaccinating adult women. We estimated the number of CIN2+ lesions using: 1) age-specific published rates of CIN2+ and proportional attribution of HPV 16/18 and HPV 31/33/45/52/58 (Gargano et al. 2018; Flagg et al. 2014; Hariri et al. 2015)<sup>25 26 27</sup>; and 2) rates of incident and incident persistent infection in the placebo groups of 4vHPV vaccine clinical trials and progression probabilities<sup>24, 28</sup> (Merck, unpublished data; Insinga et al. 2011; Skinner et al. 2016)<sup>24</sup>.

Estimates from Table 6 show an overall annual number of CIN2+ of ~200,000 caused by any HPV types. Of these, approximately 150,000 cases are caused by the 7 high-risk types in the 9vHPV vaccine, and 47% (~72,000 cases) are diagnosed in women age 30 or older annually. We assumed all HPV infections associated lesions began prior to age 27 and may have progressed within 36 months.

Estimates from Table 7 provide another perspective on HPV infections acquired prior to age 27 and associated CIN2+ lesions. Approximately 60,000 CIN2+ are caused by persistent infections acquired within the prior 24 months. Approximately 88,000 CIN2+ were estimated from incident infections that progress within 12 months, while approximately 130,000 incident infections were estimated to progress to CIN2+ within 36 months.

**Table 6: Annual Number of CIN2+ Lesions in the United States Attributed to 9vHPV Vaccine High-Risk HPV Types: Estimated from Rates of CIN2+ and Proportional Attribution of HPV Types in Lesions**

(Merck, unpublished data, attribution proportions from Hariri et al. 2015)

| Scenario | Annual Number of CIN2+ Cases |                                        |                            |               |
|----------|------------------------------|----------------------------------------|----------------------------|---------------|
|          | Any CIN2+,n                  | Attributed to HPV 16/18/31/33/45/52/58 |                            |               |
|          |                              | Any Age, n                             | Timing of Diagnosis, n (%) |               |
|          |                              |                                        | Under Age 30               | Age 30+ Years |
| 1        | 208,645                      | 155,405                                | 82,531 (53%)               | 72,874 (47%)  |
| 2        | 205,438                      | 154,052                                | 81,777 (53%)               | 72,275 (47%)  |
| 3        | 197,444                      | 148,192                                | 75,318 (51%)               | 72,874 (49%)  |

**Table 7: Annual Number of CIN2+ Lesions Attributed to 9vHPV Vaccine High Risk HPV Types in the United States: Diagnosed in Women 21-29 Years Old with Causal Infection Starting Before Age 27 (Merck, unpublished data)**

*(Estimated from HPV Incident Persistent Anogenital Infection Rates and Progression Probabilities)*

| CIN2+ After Start of Causal HPV Anogenital Infection          | Age at Diagnosis (years) |        | Total CIN2+ (16/18/31/33/45/52/58) Cases |
|---------------------------------------------------------------|--------------------------|--------|------------------------------------------|
|                                                               | 21-24                    | 25-29  |                                          |
| Within 24 months after start of incident persistent infection | 23,838                   | 36,119 | 59,957                                   |
| Within 12 months                                              | 57,660                   | 30,388 | 88,048 (within 12 months)                |
| Within 36 months                                              | 84,618                   | 45,410 | 130,028 (within 36 months)               |

### 2.9.1 Details of CIN2+ Lesion Analysis

We used recently published CIN2+ rates from the CDC's HPV-IMPACT Program<sup>25</sup> to estimate the number of persons in the US with CIN2+ lesions associated with the 9vHPV types (Table 6). We used rates for the years 2008-2009 to approximate the pre-vaccine era. Because the Gargano et al.<sup>25</sup> publication did not report rates beyond the age of 40, we used data from 3 states reported in another publication (Flagg et al. 2014<sup>26</sup>) to estimate rates for ages above 40. Specifically, we identified the percent change in rates from one age category to the next older category (Table 8). Because the 3 states had similar percent differences in each adjacent age category, we combined data for the 3 states. The percent difference in adjacent age categories in Gargano et al.<sup>25</sup> up to age 40 was similar to those of the states, so the extrapolation seemed reasonable. Thus, the CIN2+ rates for categories above 40 years old were extrapolated from the Gargano et al.<sup>25</sup> and Flagg et al.<sup>26</sup> data.

**Table 8. Rates of CIN2+ Used to Estimate Annual Number of CIN2+ Cases in the US**

| Age (years) | Annual CIN 2+ Rate (per 100,000 PY)* | Annual CIN 2+ Rate (per 100,000 PY) |       |       | Difference in Rate Percentage Between Each Adjacent Age Group |     |     |
|-------------|--------------------------------------|-------------------------------------|-------|-------|---------------------------------------------------------------|-----|-----|
|             |                                      | KY                                  | LA    | MI    | KY                                                            | LA  | MI  |
| 18-20       | 210.1                                | 58.8                                | 32.8  | 31.3  |                                                               |     |     |
| 21-24       | 584.6                                | 284.6                               | 177.1 | 185.9 | 4.8                                                           | 5.4 | 5.9 |
| 25-29       | 505.8                                | 262.7                               | 215.5 | 220.7 | 0.9                                                           | 1.2 | 1.2 |
| 30-34       | 367.0                                | 207                                 | 125.9 | 166.2 | 0.8                                                           | 0.6 | 0.8 |
| 35-39       | 221.8                                | 116.7                               | 89.1  | 97.1  | 0.6                                                           | 0.7 | 0.6 |
| 40-44       | 146.2                                | 78.5                                | 57.3  | 64.2  | 0.7                                                           | 0.6 | 0.7 |
| 45-49       | 77.8                                 | 43                                  | 28.4  | 35.5  | 0.5                                                           | 0.5 | 0.6 |
| 50-54       | 43.7                                 | 21.6                                | 17.5  | 20.1  | 0.5                                                           | 0.6 | 0.6 |
| 55-59       | 32.4                                 | 18                                  | 10.9  | 15.4  | 0.8                                                           | 0.6 | 0.8 |
| 60-64       | 28.5                                 | 14.6                                | 10    | 14.1  | 0.8                                                           | 0.9 | 0.9 |
| 65+         | 13.3                                 | 6                                   | 5.8   | 5.8   | 0.4                                                           | 0.6 | 0.4 |

\*Rates of CIN2+ in this column are from Gargano et al. 2018, except for the age groups 40-44 and older. Rates for the older categories were calculated by applying rate proportions from KY, LA, MI (derived from Flagg et al. 2014) to each successive age group, starting with the incidence rates from Gargano et al. (2018) for the age category 35-39 years old.

We used the 2007 census data to estimate the female population size for each age category of CIN2+ rates shown in Table 8. We selected census data from 2007 to approximate the number of lesions in the absence of vaccination. Because most HPV infections that lead to CIN2+ diagnoses within 36 months after detection, we assumed that all lesions diagnosed in women under 30 years old could be caused by an infection that started before age 27. We used the rates and population size to obtain the number of CIN2+ lesions diagnosed annually for each HPV type. We then estimated the number of CIN2+ lesions attributable to HPV 16/18 and HPV 31/33/45/52/58 by using attribution estimates reported by Hariri et al. 2015 (Table 9).

We also estimated 2 variations of these rates:

- 1) We used Flagg et al. rates for the age category 18-20 years because Pap testing in females under 20 years of age is now an uncommon practice and we therefore expect rates in that category to be sparse (Table 10); and

2) While CIN2+ detected in 18-20 year old women may regress, we assumed that some may persist and be detected in women 21-24 years old. Therefore, we added 100/100,000 person-years to the adjacent age category (21-24 years) (Table 11). Ultimately, these variations in assumption had little impact on the final estimates of the annual number of CIN2+ lesions.

We also used incidence rates from the young and adult women 4vHPV vaccine clinical trials (Protocol 12 and Protocol 019) and transition probabilities for infection to progress to CIN2+, using progression probabilities from Insinga et al. (2011)<sup>29</sup> and Skinner et al. (2016)<sup>24</sup> (Tables 12-13).

Our findings suggest:

- Annual number of CIN2+ cases in US caused by any HPV type: **197,444 - 208,645**
- Of these, annual number of CIN2+ cases caused by any 7 high-risk type targeted by 9vHPV vaccine: **148,192 – 155,405**, of which:
  - **75,318 – 82,531** arise from infections acquired prior to age 27
  - **72,275 - 72,874** arise from infections acquired at age 27 years or older

In models used to calculate the number of lesions from rates of HPV infections and probabilities of progression, we estimate that approximately 59,957 CIN2+ cases are caused by persistent infections acquired within the prior 24 months. Approximately 88,048 CIN2+ were estimated from incident infections that progress within 12 months, and approximately 130,028 incident infections were estimated to progress to CIN2+ within 36 months. We note that the number of CIN2+ using the 12 month progression probabilities (88,048) is quite similar to the annual number of CIN2+ cases noted above for women under 27 years old at the time of their causal HPV infection. Also noteworthy is the consistency between these estimates and the median age at HPV infection acquisition described below.



**Table 9: Rates and Variables Used to Estimate Annual Number of CIN2+ Lesions in United States**

Rates from Gargano et al. (2018) and Rates for Ages 40+ Extrapolated From State-Level Data (Scenario 1)

| Age   | Annual CIN2+ Rate (per 100,000 py) | Female Population | Estimated Annual Number of CIN2+ (all HPV types) | Fraction of CIN2+ Attributable to 16/18 | Fraction of CIN2+ Attributable to 31/33/45/52/58 | Annual Number of CIN2+ Attributed to 16/18 | Annual Number of CIN2/3 Attributed to 31/33/45/52/58 | Total Annual Number of CIN2+ Attributed to 9v HPV Vaccine Types | Annual Number of CIN2+ Attributed to 9v HPV Vaccine Types in Females <30 Years Old |
|-------|------------------------------------|-------------------|--------------------------------------------------|-----------------------------------------|--------------------------------------------------|--------------------------------------------|------------------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------------------------|
| 18-20 | 210.1                              | 6,623,831         | 13,917                                           | 44.0                                    | 20.4                                             | 6,123                                      | 2,839                                                | 155,405                                                         | 82,531 (53% of Total)                                                              |
| 21-24 | 584.6                              | 7,994,408         | 46,735                                           | 50.0                                    | 23.3                                             | 23,368                                     | 10,889                                               |                                                                 |                                                                                    |
| 25-29 | 505.8                              | 10,213,106        | 51,658                                           | 51.6                                    | 24.5                                             | 26,655                                     | 12,656                                               |                                                                 |                                                                                    |
| 30-34 | 367.0                              | 9,574,861         | 35,140                                           | 50.8                                    | 25.8                                             | 17,851                                     | 9,066                                                |                                                                 |                                                                                    |
| 35-39 | 221.8                              | 10,452,497        | 23,184                                           | 42.4                                    | 32.7                                             | 9,830                                      | 7,581                                                |                                                                 |                                                                                    |
| 40-44 | 146.2                              | 10,865,786        | 15,882                                           | 42.4                                    | 32.7                                             | 6,734                                      | 5,193                                                |                                                                 |                                                                                    |
| 45-49 | 77.8                               | 11,589,264        | 9,014                                            | 42.4                                    | 32.7                                             | 3,822                                      | 2,947                                                |                                                                 |                                                                                    |
| 50-54 | 43.7                               | 10,956,785        | 4,786                                            | 42.4                                    | 32.7                                             | 2,029                                      | 1,565                                                |                                                                 |                                                                                    |
| 55-59 | 32.4                               | 9,507,391         | 3,076                                            | 42.4                                    | 32.7                                             | 1,304                                      | 1,006                                                |                                                                 |                                                                                    |
| 60-64 | 28.5                               | 7,959,500         | 2,270                                            | 42.4                                    | 32.7                                             | 962                                        | 742                                                  |                                                                 |                                                                                    |
| 65+   | 13.3                               | 22,390,442        | 2,985                                            | 42.4                                    | 32.7                                             | 1,265                                      | 976                                                  |                                                                 |                                                                                    |

**Table 10: Rates and Variables Used to Estimate Annual Number of CIN2+ Lesions in United States**

Rates from Gargano et al. (2018) with Modifications (Scenario 2)

(Rates for ages 18-20 and 40+ used data from Flagg et al. (2014), and a higher rate of CIN2+ was Used for ages 21-24, assuming more females would be entering screening at those ages rather than ages 18-20.)

| Age   | CIN2+ Rate (per 100,000 py) | Female Population | Estimated Annual Number of CIN2+ (all HPV types) | Fraction of CIN2+ Attributable to 16/18 | Fraction of CIN2+ Attributable to 31/33/45/52/58 | Annual Number of CIN2+ Attributed to 16/18 | Annual Number of CIN2/3 Attributed to 31/33/45/52/58 | Annual Number of CIN2+ Attributed to HPV 16/18/31/33/45/52/58 | Annual Number of CIN2+ Attributed to HPV 16/18/31/33/45/52/58 in Females <30 Years Old | Proportion of CIN2+ Attributed to HPV 16/18/31/33/45/52/58 in Females <30 Years Old |
|-------|-----------------------------|-------------------|--------------------------------------------------|-----------------------------------------|--------------------------------------------------|--------------------------------------------|------------------------------------------------------|---------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| 18-20 | 41                          | 6,623,831         | 2,716                                            | 44.0                                    | 20.4                                             | 1,195                                      | 554                                                  |                                                               |                                                                                        |                                                                                     |
| 21-24 | 684.6                       | 7,994,408         | 54,730                                           | 50.0                                    | 23.3                                             | 27,365                                     | 12,752                                               |                                                               |                                                                                        |                                                                                     |
| 25-29 | 505.8                       | 10,213,106        | 51,658                                           | 51.6                                    | 24.5                                             | 26,655                                     | 12,656                                               |                                                               |                                                                                        |                                                                                     |
| 30-34 | 367.0                       | 9,574,861         | 35,140                                           | 50.8                                    | 25.8                                             | 17,851                                     | 9,066                                                |                                                               |                                                                                        |                                                                                     |
| 35-39 | 221.8                       | 10,452,497        | 23,184                                           | 42.4                                    | 32.7                                             | 9,830                                      | 7,581                                                |                                                               |                                                                                        |                                                                                     |
| 40-44 | 146.2                       | 10,865,786        | 15,882                                           | 42.4                                    | 32.7                                             | 6,734                                      | 5,193                                                | 154,052                                                       | 81,177                                                                                 | 53%                                                                                 |
| 45-49 | 77.8                        | 11,589,264        | 9,014                                            | 42.4                                    | 32.7                                             | 3,822                                      | 2,947                                                |                                                               |                                                                                        |                                                                                     |
| 50-54 | 43.7                        | 10,956,785        | 4,786                                            | 42.4                                    | 32.7                                             | 2,029                                      | 1,565                                                |                                                               |                                                                                        |                                                                                     |
| 55-59 | 32.4                        | 9,507,391         | 3,076                                            | 42.4                                    | 32.7                                             | 1,304                                      | 1,006                                                |                                                               |                                                                                        |                                                                                     |
| 60-64 | 28.5                        | 7,959,500         | 2,270                                            | 42.4                                    | 32.7                                             | 962                                        | 742                                                  |                                                               |                                                                                        |                                                                                     |
| 65+   | 13.3                        | 22,390,442        | 2,985                                            | 42.4                                    | 32.7                                             | 1,265                                      | 976                                                  |                                                               |                                                                                        |                                                                                     |

**Table 11: Rates and Variables Used to Estimate Annual Number of CIN2+ Lesions in United States**

Rates from Gargano et al. (2018) with Modifications (Scenario 3) (Rates for ages 18-20 and 40+ used data from Flagg et al. (2014), assuming more females would be entering screening at those ages rather than at ages 18-20.)

| Age   | Annual CIN2+ Rate (per 100,000 py) | Female Population | Estimated Annual Number of CIN2+ (all HPV types) | Fraction of CIN2+ Attributable to 16/18 | Fraction of CIN2+ Attributable to 31/33/45/52/58 | Annual Number of CIN2+ Attributed to 16/18 | Annual Number of CIN2/3 Attributed to 31/33/45/52/58 | Annual Number of CIN2+ Attributed to HPV 16/18/31/33/45/52/58 | Annual Number of CIN2+ Attributed to HPV 16/18/31/33/45/52/58 in Females <30 Years Old | Proportion of CIN2+ Attributed to HPV 16/18/31/33/45/52/58 in Females <30 Years Old |
|-------|------------------------------------|-------------------|--------------------------------------------------|-----------------------------------------|--------------------------------------------------|--------------------------------------------|------------------------------------------------------|---------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| 18-20 | 41                                 | 6,623,831         | 2,716                                            | 44.0                                    | 20.4                                             | 1,195                                      | 554                                                  |                                                               |                                                                                        |                                                                                     |
| 21-24 | 584.6                              | 7,994,408         | 46,735                                           | 50.0                                    | 23.3                                             | 23,368                                     | 10,889                                               |                                                               |                                                                                        |                                                                                     |
| 25-29 | 505.8                              | 10,213,106        | 51,658                                           | 51.6                                    | 24.5                                             | 26,655                                     | 12,656                                               |                                                               |                                                                                        |                                                                                     |
| 30-34 | 367.0                              | 9,574,861         | 35,140                                           | 50.8                                    | 25.8                                             | 17,851                                     | 9,066                                                |                                                               |                                                                                        |                                                                                     |
| 35-39 | 221.8                              | 10,452,497        | 23,184                                           | 42.4                                    | 32.7                                             | 9,830                                      | 7,581                                                |                                                               |                                                                                        |                                                                                     |
| 40-44 | 146.2                              | 10,865,786        | 15,882                                           | 42.4                                    | 32.7                                             | 6,734                                      | 5,193                                                | 148,192                                                       | 75,318                                                                                 | 51%                                                                                 |
| 45-49 | 77.8                               | 11,589,264        | 9,014                                            | 42.4                                    | 32.7                                             | 3,822                                      | 2,947                                                |                                                               |                                                                                        |                                                                                     |
| 50-54 | 43.7                               | 10,956,785        | 4,786                                            | 42.4                                    | 32.7                                             | 2,029                                      | 1,565                                                |                                                               |                                                                                        |                                                                                     |
| 55-59 | 32.4                               | 9,507,391         | 3,076                                            | 42.4                                    | 32.7                                             | 1,304                                      | 1,006                                                |                                                               |                                                                                        |                                                                                     |
| 60-64 | 28.5                               | 7,959,500         | 2,270                                            | 42.4                                    | 32.7                                             | 962                                        | 742                                                  |                                                               |                                                                                        |                                                                                     |
| 65+   | 13.3                               | 22,390,442        | 2,985                                            | 42.4                                    | 32.7                                             | 1,265                                      | 976                                                  |                                                               |                                                                                        |                                                                                     |



**Table 12: Annual Number of CIN2+ Lesions Attributed to HPV 16/18/31/33/45/52/58 in the United States Diagnosed in Women 21-29 Years Old**

*Estimated from HPV Anogenital Persistent Infection Incidence Rates and Progression Probabilities)*

| HPV Type                                                                                              | 16                       | 18         | 31                                       | 33         | 45         | 52         | 58         |
|-------------------------------------------------------------------------------------------------------|--------------------------|------------|------------------------------------------|------------|------------|------------|------------|
| <b>Women &lt;25 Years Old at Causal Infection</b>                                                     |                          |            |                                          |            |            |            |            |
| Incidence of Anogenital Infection (per 100 person-years)                                              | 5.35                     | 1.77       | 2.34                                     | 0.76       | 1.06       | 2.86       | 1.64       |
| Population Size                                                                                       | 7,994,408                | 7,994,408  | 7,994,408                                | 7,994,408  | 7,994,408  | 7,994,408  | 7,994,408  |
| # New Anogenital Infections in 12 Months                                                              | 427,790                  | 141,412    | 186,891                                  | 60,402     | 84,563     | 228,818    | 130,753    |
| Probability of Infection Progressing to CIN2+                                                         |                          |            |                                          |            |            |            |            |
| 12 months                                                                                             | 6.8                      | 1.6        | 6                                        | 4.7        | 2.2        | 2.2        | 4.1        |
| 36 months                                                                                             | 9.3                      | 4          | 8.6                                      | 13.2       | 2.2        | 2.2        | 6.3        |
| # New CIN2+ Lesions                                                                                   |                          |            |                                          |            |            |            |            |
| 12 months                                                                                             | 29,090                   | 2,263      | 11,213                                   | 2,839      | 1,860      | 5,034      | 5,361      |
| 36 months                                                                                             | 39,784                   | 5,656      | 16,073                                   | 7,973      | 1,860      | 5,034      | 8,237      |
| <b>Women 25-29 Years Old at Causal Infection</b>                                                      |                          |            |                                          |            |            |            |            |
| Incidence of Anogenital Infection (per 100 person-years)                                              | 2.08                     | 0.82       | 0.64                                     | 0.43       | 0.72       | 1.26       | 1.00       |
| Population Size                                                                                       | 10,213,106               | 10,213,106 | 10,213,106                               | 10,213,106 | 10,213,106 | 10,213,106 | 10,213,106 |
| # infections                                                                                          | 212,543                  | 84,189     | 64,867                                   | 44,165     | 73,148     | 128,354    | 102,131    |
| Probability of Infection Progressing to CIN2+                                                         |                          |            |                                          |            |            |            |            |
| 12 months                                                                                             | 6.8                      | 1.6        | 6                                        | 4.7        | 2.2        | 2.2        | 4.1        |
| 36 months                                                                                             | 9.3                      | 4          | 8.6                                      | 13.2       | 2.2        | 2.2        | 6.3        |
| # New CIN2+ Lesions                                                                                   |                          |            |                                          |            |            |            |            |
| 12 months                                                                                             | 14,453                   | 1,347      | 3,892                                    | 2,076      | 1,609      | 2,824      | 4,187      |
| 36 months                                                                                             | 19,767                   | 3,368      | 5,579                                    | 5,830      | 1,609      | 2,824      | 6,434      |
| <b>Women 21-29 Years Old at CIN2+ Diagnosis<br/>Causal Infection Occurring Before 27 Years of Age</b> |                          |            |                                          |            |            |            |            |
| Time to CIN2+ After Start of Causal HPV Anogenital Infection                                          | Age at Diagnosis (years) |            | Total CIN2+ (16/18/31/33/45/52/58) Cases |            |            |            |            |
|                                                                                                       | 21-24                    | 25-29      |                                          |            |            |            |            |
| Within 12 months                                                                                      | 57,660                   | 30,388     | <b>88,048 (within 12 months)</b>         |            |            |            |            |
| Within 36 months                                                                                      | 84,618                   | 45,410     | <b>130,028 (within 36 months)</b>        |            |            |            |            |

**Table 13: Annual Number of CIN2+ Lesions Attributed to HPV 16/18/31/33/45/52/58 in the United States Diagnosed in Women 21-29 Years Old**

*(Estimated from HPV Type-Specific Anogenital Persistent Infection Incidence Rates and Progression Probabilities)*

| HPV Type                                                                                                             | 16                       | 18         | 31                                           | 33         | 45         | 52         | 58         |
|----------------------------------------------------------------------------------------------------------------------|--------------------------|------------|----------------------------------------------|------------|------------|------------|------------|
| <b>Females 21-24 Years Old</b>                                                                                       |                          |            |                                              |            |            |            |            |
| Persistent Incident Infection (PI) Rates (per 100 person-years)                                                      | 4.14                     | 0.05       | 0.06                                         | 0.02       | 0.03       | 0.06       | 0.03       |
| Population size                                                                                                      | 7994408                  | 7994408    | 7994408                                      | 7994408    | 7994408    | 7994408    | 7994408    |
| # Persistent Infections                                                                                              | 330,633                  | 3,771      | 4,829                                        | 1,720      | 2,001      | 4,741      | 2,398      |
| 24 month Progression Probability                                                                                     | 15                       | 6          | 8                                            | 30         | 8          | 4          | 4          |
| # CIN2+ Within 24 Months After Start of PI                                                                           | 49,595                   | 226        | 386                                          | 516        | 160        | 190        | 96         |
| <b>Females 25-29 Years Old</b>                                                                                       |                          |            |                                              |            |            |            |            |
| Persistent Incident Infection (PI) Rates (/100 person-yr)                                                            | 1.3                      | 0.4        | 0.4                                          | 0.1        | 0.3        | 0.6        | 0.3        |
| Population Size                                                                                                      | 10,213,106               | 10,213,106 | 10,213,106                                   | 10,213,106 | 10,213,106 | 10,213,106 | 10,213,106 |
| # Persistent Infections                                                                                              | 136,635                  | 44,165     | 40,024                                       | 11,041     | 33,124     | 62,107     | 33,124     |
| # CIN2+ Within 24 Months after Start of PI                                                                           | 13,527                   | 1,749      | 2,113                                        | 2,186      | 1,749      | 1,640      | 874        |
| <b>HPV 6/11/16/18/31/33/45/52/58-Related CIN2+ Diagnosis Assuming Causal Infection Starts Before 27 Years of Age</b> |                          |            |                                              |            |            |            |            |
| # CIN2+ After Start of Causal HPV Anogenital PI Infection                                                            | Age at Diagnosis (years) |            | Total CIN2+ (HPV 16/18/31/33/45/52/58) Cases |            |            |            |            |
|                                                                                                                      | 21-24                    | 25-29      |                                              |            |            |            |            |
| Within 24 Months                                                                                                     | 23,838                   | 36,119     | <b>59,957</b>                                |            |            |            |            |

### 3 Cost-effectiveness analysis of 9vHPV in 27-45 year olds

We focused our evaluation on comparison of the Merck model and the CDC simplified model since we do not have all the details of the HPV-ADVISE model. An initial comparison of Merck's model with CDC's simplified model showed significant differences in cost-effectiveness results (85,205\$/QALY for Merck, versus 492,500\$/QALY for CDC). Compared to the CDC simplified model, the Merck model predicts more disease averted, and lower incremental cost-effectiveness ratio (ICER) for mid-adult vaccination. Each of the models makes somewhat different assumptions about the implementation of the MAP vaccination strategy (inclusion of historical vaccination period, assumed mid-adult vaccination uptake, series completion, etc.), however, these differences are not sufficient to account for these large differences in

outcomes. It is necessary to investigate the reasons for these discrepancies. This is a matter of public health significance in the US, where teenage vaccine coverage rates remain below target goals<sup>30</sup>, and MAPs remain susceptible to HPV infection, and subsequent HPV-related diseases.

### *3.1 Cost-effectiveness results*

In the cost-effectiveness model, we compared status quo vaccination with MAP vaccination. The status quo strategy assumes current routine and catch-up ACIP recommendations for 9-26 year-old female and 9-21 year-old male vaccination remain in place. The MAP strategy assumes the current ACIP recommendation is extended to include 9-45 year old females and males with an additional adult vaccination uptake of 2.6% and 1.9% for females and males, respectively. In order to facilitate model comparison, we modified our input parameters to match the CDC simplified model input parameters as follows:

1. We used the NIS-Teen 2014-2015 3-dose vaccine coverage rates (instead of NHANES), without historical coverage
2. Persons  $\geq 15$  years old received 3 doses and all persons 9-14 years old received 2 doses of the vaccine
3. We assumed full vaccine completion for all cohorts
4. We assumed a total population size of 322.899 million people as used in the CDC simplified model in Merck's model. We modified our MAP strategy to match the number of persons vaccinated (~350 million) over the time horizon and the vaccination costs to that in the CDC simplified model.

The ICERs for MAP vaccination compared with status quo for the CDC simplified model and Merck model were estimated at \$492,500/QALY and 88,450\$/QALY, respectively (Table 14). The main reason for the discrepancy in ICERs is most likely that the Merck model estimated 55,768 cancers averted, higher than that estimated by the CDC simplified model at 34,800 cancers averted. This resulted in more QALYs gained and thus a lower ICER for the Merck model.

**Table 14: Comparison of CDC simplified model and Merck model (using similar assumptions)**

| Item estimated                                         | CDC Model           |                      |             | Merck Model        |                     |             |
|--------------------------------------------------------|---------------------|----------------------|-------------|--------------------|---------------------|-------------|
|                                                        | Status Quo          | MAP vaccination      | Difference  | Status Quo         | MAP vaccination     | Difference  |
| Millions vaccinated                                    | 286.6               | 346.8                | 60.2        | 283.2              | 349.5               | 61.9        |
| As % of status quo                                     |                     |                      | 21.0%       |                    |                     | 21.9%       |
| Vaccination costs (per-capita)                         | 141.3               | 205.5                | 64.2        | 155.0              | 215.9               | 60.9        |
| Cancers averted in females                             | 957,400             | 977,400              | 20,000      | 773,075            | 803,170             | 30,095      |
| Cancers averted in males                               | 491,700             | 506,600              | 14,800      | 364,167            | 389,840             | 25,673      |
| Total cancers averted                                  | 1,449,200           | 1,484,000            | 34,800      | 1,137,242          | 1,193,009           | 55,768      |
| Direct medical costs averted (per-capita)              | 89.6                | 92.6                 | 3.0         | 124.8              | 132.5               | 7.7         |
| Number of QALYs gained vs. no vaccination (per-capita) | 0.00357936          | 0.00370366           | 0.000124302 | 0.00918976         | 0.00979001          | 0.000600347 |
| Incremental cost per QALY gained (\$/QALY)             | 14,400 <sup>‡</sup> | 492,500 <sup>†</sup> |             | 3,204 <sup>‡</sup> | 88,450 <sup>†</sup> |             |

<sup>‡</sup> ICER for status quo compared with no vaccination

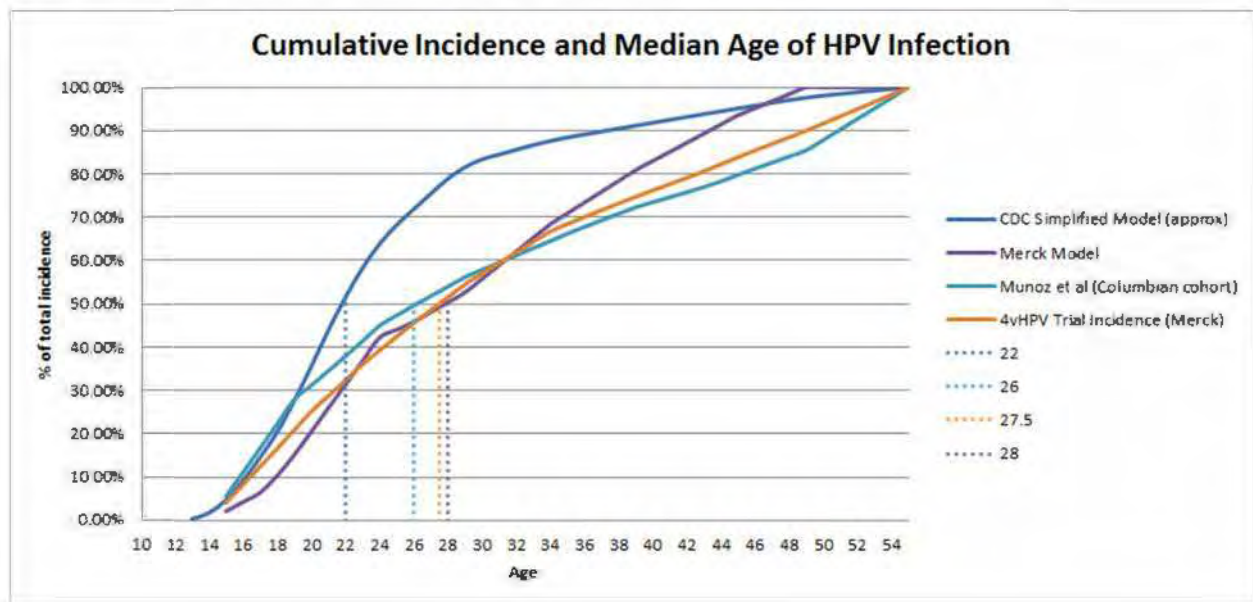
<sup>†</sup> ICER for MAP vaccination compared with status quo

### 3.2 Median age of HPV infection

- Understanding the median age at which incidence of infection occurs can help us understand whether infection occurs among MAPs. A lower median age of infection implies a higher proportion of persons are already infected and, therefore, deriving limited benefit from vaccination.
- We estimated median age of first HPV infection to be 27 years. The cumulative incidence of HPV infection by age as estimated by the Merck model is plotted in Figure 4.
- Using HPV-acquisition probabilities in the CDC simplified model, we generated a curve of cumulative incidence for HPV-16 type infection with age (also plotted in Figure 4). An approximate estimate of the median age in the CDC simplified model is 22 years (Figure 4).
- We used incidence rates (
- Table 15) for women in the placebo group from 4vHPV<sup>31,32,33,34</sup> trials and from the Colombian cohort<sup>35</sup> and applied them to the 2017 US population to estimate the annual incident HPV infection in the US, and added the resultant estimated cumulative annual incident HPV infection by age curve to Figure 4.
- We found that the slope of the HPV cumulative incidence is much steeper in the CDC simplified model during younger ages and becomes flatter after age 27, compared to that in the Merck model. The cumulative incidence curves plotted from annual incidence rates in the 4vHPV and Colombian cohort match the Merck curve closely, with the median age of infection closer to 27 years than 22 years.
- Assuming that similar proportions of HPV infections progress to cancer for persons below and above 27 years of age, and assuming a 30-40 year period for a HPV infection to progress to cancer,

and life-expectancy of 36.1 years at age 45,<sup>36</sup> the median age of infection that results in cancer is likely to be closer to 27 years, rather than 20.6 years as estimated by Burger et al.<sup>37</sup>

**Figure 4: Cumulative annual incidence of HPV infection**



**Table 15. Incidence rates of High-Risk HPV (any type) among women from 4vHPV clinical trials and Columbian cohort**

| Age group | 4vHPV trial (placebo) | Age group | Columbian cohort <sup>*</sup> |
|-----------|-----------------------|-----------|-------------------------------|
| 16-20     | 16.01                 | 15-19     | 14.7                          |
| 21-24     | 12.81                 | 20-24     | 8.3                           |
| 24-29     | 10.93                 | 25-29     | 5.5                           |
| 30-34     | 9.07                  | 30-34     | 4.3                           |
| 35-39     | 6.34                  | 35-39     | 4.2                           |
| 40-44     | 6.01                  | 40-44     | 3.3                           |
|           |                       | 45-49     | 3.8                           |
|           |                       | 50-54     | 6.0                           |

<sup>\*</sup> Digitized plot from Munoz et al

### 3.3 History of convergence of cost-effectiveness models for younger cohorts

- The CDC simplified model<sup>38</sup>, HPV-ADVISE model<sup>39</sup>, and Merck model<sup>40</sup>, have been extensively peer-reviewed in top-tier journals.
- The three models have always produced similar results during evaluation of the cost-effectiveness of HPV vaccine in 5 previous evaluations presented at ACIP meetings.<sup>41,42,43,44,45</sup>
- The Merck model was one of the first published models in the field of HPV vaccination and a significant contribution to the literature with over 400 citations. All the equations and parameters used in the models have been published.<sup>46</sup>

- Merck model has also been cross-validated using other models.
  - In a systematic review and meta-analysis of model predictions from transmission-dynamic models of the long-term population-level effectiveness of vaccination against HPV, Brisson et al<sup>47</sup> examined the variability in predicted herd effects, incremental benefit of vaccinating boys, and potential for HPV-vaccine-type elimination. They found 16 eligible models, including the Merck model, that provided predictions. They concluded that although HPV models differ in structure, data used for calibration, settings, and population-level predictions were generally concordant.
  - In a literature review conducted to evaluate models of HPV vaccination in terms of their capacity, requirements, limitations and comparability, Jit et al<sup>48</sup> found 6 models (including the Merck model) that were used to evaluate the cost-effectiveness of HPV vaccination of adolescent girls. Despite differences in model type, structure, assumptions and complexity, the authors reached conclusions that were qualitatively similar about the cost-effectiveness of vaccination, although they displayed diverse quantitative features particularly in sensitivity analyses.
- Given the history of convergence during previous evaluations of cost-effectiveness of HPV vaccine for the ACIP and with other models in lower age groups, and lack of any structural changes in the Merck model in the current version, it may be helpful to understand the reasons for differences in the results from the three models for the mid-adult cost-effectiveness analysis.

## 4 Differences in models

Several variables that may explain the differences in the cost effectiveness results include the model structure, the probability of HPV acquisition, and the duration of progression from CIN3 to cancer.

### 4.1 Model structure

- The CDC simplified model is a Susceptible Infected (SI) model that assumes that people infected cannot be re-infected after a first infection.
- The Merck model is a Susceptible-Infected-Recovery-Susceptible (SIRS) model that considers that individuals infected by HPV have a probability to recover and are then susceptible to be infected again.
- Several HPV natural history studies have suggested that individuals can be re-infected with the same type after apparently having cleared their HPV infection.<sup>49,50,51</sup> This difference between the two models could be important and may reduce the number of susceptible MAPs in the CDC simplified model compared with the Merck model, and consequently the number of incident HPV infections and associated HPV-related diseases among MAPs.
- The Merck model makes detailed assumptions about seroconversion and natural immunity after infection<sup>52,53,54</sup>. These assumptions are presented in
  -
- Table 16.
  - The assumptions about the degree of protection in individuals with measurable levels of naturally acquired antibodies are consistent with findings from a recent meta-analysis by Bleacher et al. (2016),<sup>55</sup> which reported that seropositive females have significant, but modest protection against subsequent genital HPV 16 infections (pooled relative risk [RR]: 0.65; IC<sub>95%</sub>: 0.5-0.8) and HPV 18 (pooled RR: 0.7; IC<sub>95%</sub>: 0.43-0.98) infections compared to seronegative females. Among men, seropositivity was not associated with significant protection against future HPV 16 or 18 genital infections. These findings confirm that even among individuals with measurable HPV antibodies (of note, only a proportion of



individuals seroconvert after an HPV infection), subsequent HPV infections should be considered in an HPV natural disease model.

**Table 16: Parameters of natural history of HPV disease**

| Parameters                                                                                                   | HPV 16,18,31,33,45,52,58 |
|--------------------------------------------------------------------------------------------------------------|--------------------------|
| Fraction of people seroconvert following an anogenital HPV infection                                         |                          |
| Male                                                                                                         | 0.6                      |
| Female                                                                                                       | 0.6                      |
| Degree of protection against anogenital HPV infections provided by natural immunity following seroconversion |                          |
| Male                                                                                                         | 0.5                      |
| Female                                                                                                       | 0.8                      |

Further evidence for the susceptibility of previously exposed individuals for re-infection with the same HPV type comes from HPV clinical studies. These studies also provide evidence that HPV vaccines can reduce the rate of persistent infections or cervical/genital disease related to the HPV type for which the subjects had serological evidence of prior exposure. In the Protocol 019 trial (FUTURE III), the 4vHPV vaccine provided efficacy against HPV 6/11/16/18-related persistent infection or cervical and external genital lesions among mid-adult women who were at baseline seropositive and DNA negative to the specific HPV type in question (

Table 17).<sup>56</sup> A similar finding among young women participating in the FUTURE I and II studies of 4vHPV was reported by Olsson et al.<sup>57</sup>

**Table 17: Efficacy against HPV6/11/16/18-related persistent infection and disease in seropositive and PCR-negative subjects in clinical trials of 4vHPV vs placebo<sup>58</sup>**

| Endpoint                                               | 4vHPV vaccine (N=1910) |       |        |      | Placebo (N=1907) |       |        |      | Observed efficacy (%) | 95% CI         |
|--------------------------------------------------------|------------------------|-------|--------|------|------------------|-------|--------|------|-----------------------|----------------|
|                                                        | N                      | Cases | PYR    | Rate | N                | Cases | PYR    | Rate |                       |                |
| HPV 6/11/16/18-related persistent infection, CIN/EGL   | 506                    | 5     | 1882.3 | 0.3  | 513              | 15    | 1868.0 | 0.8  | 66.9                  | (4.3, 90.6)    |
| <i>By HPV type and age group</i>                       |                        |       |        |      |                  |       |        |      |                       |                |
| HPV 6/11/16/18-related persistent infection (all ages) | 496                    | 5     | 1793.9 | 0.3  | 505              | 15    | 1788.7 | 0.8  | 66.8                  | (3.8, 90.5)    |
| 24-34 year olds                                        | 258                    | 3     | 909.9  | 0.3  | 248              | 4     | 880.6  | 0.5  | 27.4                  | (-329.0, 89.4) |
| 35-45 year olds                                        | 238                    | 2     | 884.0  | 0.2  | 257              | 11    | 908.2  | 1.2  | 81.3                  | (14.4, 98.0)   |

Abbreviations: CI= confidence interval; CIN =cervical intraepithelial neoplasia; EGL= external genital lesion; NA= not applicable; PYR= person years at risk; 4vHPV= quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant



vaccine; rate = incidence rate per 100 person-years at risk. N=Number of subjects randomized to the respective vaccination group who received at least 1 injection and were seropositive and DNA negative for the relevant vaccine HPV type at enrolment. n=Number of subjects who have at least one follow-up visit after Day 1.

## 4.2 HPV acquisition/ transmission

A summary of the HPV acquisition assumptions in each of the 3 models follows.

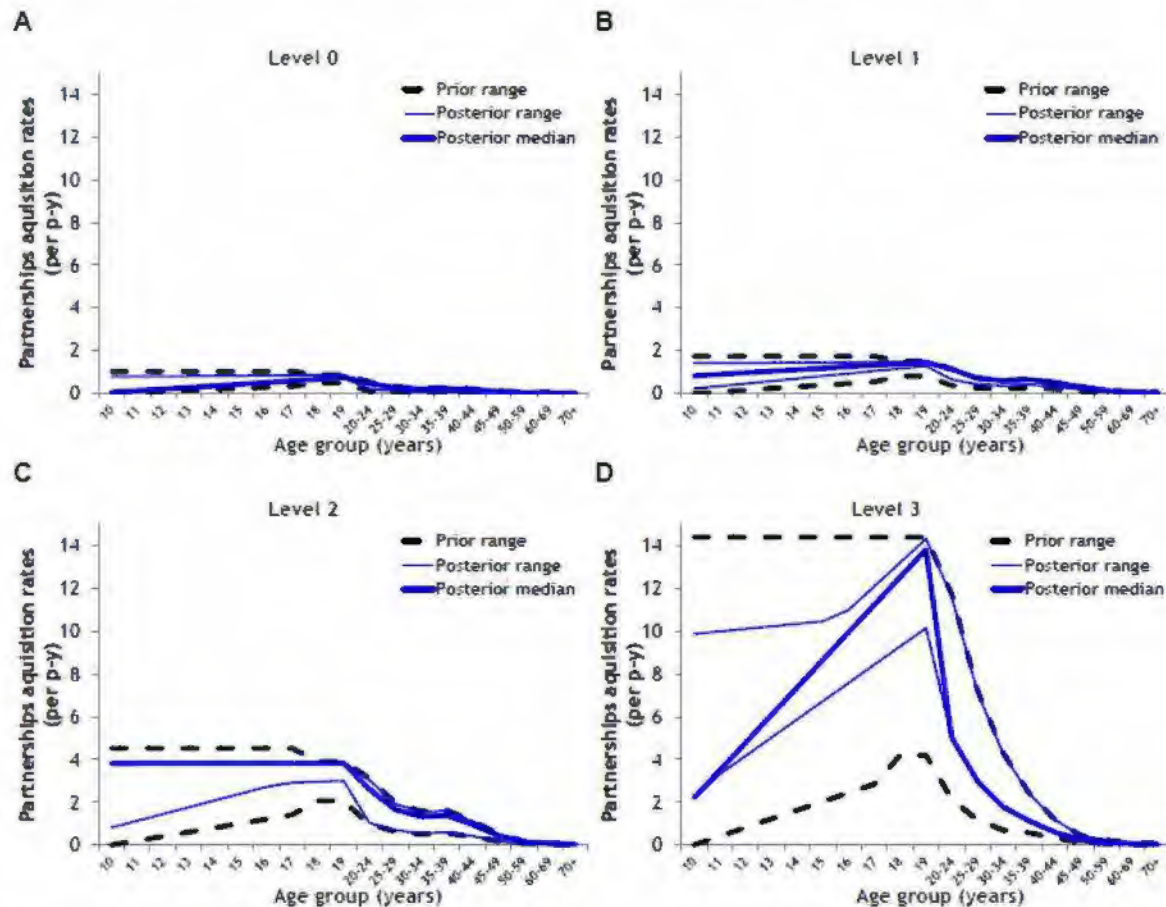
### 4.2.1 HPV-acquisition in the CDC simplified model

- In the CDC simplified model, the probability of HPV acquisition is an input to the model. The CDC simplified model uses HPV acquisition probabilities from model-based analysis by Canfell et al (2004)<sup>59</sup>, which sources transmission rates from Barnabas et al (2004)<sup>60</sup>, Melkert et al (1993)<sup>61</sup>, and Schiffman et al (2003)<sup>62</sup>, and model-based analysis by Myers et al (2000)<sup>63</sup>, which sources transmission rates from Kiviat et al (1996)<sup>64</sup>, Ho et al (1998),<sup>65</sup> and Hildesheim et al (1994)<sup>66</sup>.
- The annual HPV acquisition probability in the CDC simplified model is 0.0431, 0.0141, and 0.0065 in 20, 30, and 35 year olds, respectively.
- The HPV acquisition probabilities for MAPs in the CDC Simplified Model are much lower than those in the 4vHPV and Columbian cohort (Table 15).
- Lower HPV acquisition probabilities for MAPs are likely to result in less infection and show reduced clinical and economic impact of MAP vaccination.

### 4.2.2 HPV-acquisition in the HPV-ADVISE model

- HPV-ADVISE is an individual simulation model. Each individual or agent has multiple attributes, such as gender, age, and ability to form partnerships, HPV status, etc. This structure provides flexibility in modeling but requires more data and more complex assumptions. Therefore, calibration can be challenging, and overall individual simulation models are less tractable than differential equation-based transmission dynamic models. The complexity of the HPV-ADVISE model is demonstrated by the number of inputs required to determine the overall level of sexual activity, including:
  1. Level of sexual activity (low, l=0 with 0-1 lifetime partners, to high, l=3 with 40+ lifetime partners)
  2. Initiation of sexual activity at a rate that depends on age and level of sexual activity
  3. Partner acquisition rate which is then attributed to each sexual activity level by age
  4. A stochastic pair formation and separation process, driven by females. Each woman has a specific rate of either forming a new partnership, if single, or separating, if currently involved in a stable partnership. Only monogamous stable and casual partnerships are modeled; concurrent partnerships are not simulated
  5. A mixing matrix that enables females to select a male partner reflecting individual preferences for age and sexual activity level
- The HPV-ADVISE model uses data from the US NSFG 2006-2010 and PISCES, a Canadian survey. Partner acquisition rates were calculated from the Seattle Sex Survey.
- The complexity of the model is demonstrated in the prior range and posterior ranges for partner acquisition of sexually active males. The HPV-ADVISE model shows substantial (and non-smooth) declines in partner acquisition after age 24, even for persons with the highest risk level, defined as those with 40+ life partners (Figure 5)
- **Figure 5:** An examination of the outputs for posterior ranges in the HPV-ADVISE model appendix<sup>67</sup> shows substantial decline in sexual activity after age 24, which is not commensurate with the data from the US NSFG described previously.

Figure 5: Partner acquisition rates of sexually active males in the HPV-ADVISE model



Excerpt from HPV-ADVISE Technical Appendix. Sexual activity levels A:I=0, B:I=1, C:I=2, D:I=3. Dashed black lines represent minimums and maximums of prior ranges over age, Blue lines represent the medians, minimums, and maximums of the posterior parameter sets.

The HPV-ADVISE model also uses a narrower mixing matrix compared to what was seen in the NSFG.

The HPV-ADVISE model allows sexual mixing in a very narrow population range. For women age 20-24 with sexual activity level 0 in the HPV-ADVISE model, only 5% had sexual activity with 25-29 year old men, and 1% had activity with 30-34 year old men. Among those with activity level 2,3 only 11% had activity with 25-29 year old men, and 2% had activity with 30-34 year old men. This is lower than 17.1% of 20-24 year old women who reported having a male partner six years or older.<sup>68</sup>

#### 4.2.3 HPV-acquisition in the Merck model

- In the Merck model, transmission is determined within the model, similar to the HPV-ADVISE model.
- Transmission is based on the number of sexual partners in the previous year, using data from both men and women.
- HPV-ADVISE model uses women's sexual behavior as a starting point and use a narrow mixing matrix to define relationships with men. HPV-ADVISE assume no concurrency (simultaneous multiple partnerships). The Merck model. We use both female and male data and balances partnerships by taking the geometric mean of the total number of partnerships. The Merck model models sexual partnerships as instantaneous contacts based on number of sexual partnerships in the previous year.
- The Merck model uses three inputs for HPV acquisition:
  1. Proportion of population in each of the following sexual activity categories: Low (number of partners/year:  $\leq 1$ ), Medium (number of partners/year: 2-4), High (number of partners/year: 5+)
  2. Mean number of partners/year by activity category and gender: Low, Medium, High
  3. Sexual mixing among members of different age cohorts. The Merck model allows for broader mixing compared to that in the US NSFG.

#### 4.2.4 Summary of HPV-acquisition/transmission across the 3 models

- The HPV acquisition data and modeling are different in all three models. Given that the median age of infection is lower in the CDC and HPV-ADVISE models compared with the Merck model, the level of sexual activity among MAPs in the HPV-ADVISE model seems to be much lower than that in the Merck model.
- Understanding HPV acquisition and modeling of sexual behavior is important to understand the differences in the model.

### 4.3 *Duration of progression from CIN3 to cervical cancer*

- The HPV-ADVISE model and the Merck model have different duration of progression from CIN3 to cervical cancer.
- In the HPV-ADVISE model, the duration of progression from CIN3 to cervical cancer is based on a Gamma distribution with range of 25 to 40 years for all HPV types. The rationale for this value is not published.
- In the Merck model, the duration is about 21 years for HPV 16/18 and 35 years for other high-risk types. When the model was initially parameterized, we were unable to find values in the literature for this duration and are unaware of any published data on this topic in recent years. Therefore, we used calibration to estimate the rate from carcinoma in-situ to squamous cell carcinoma.<sup>69</sup>
- Having a higher duration of progression from CIN3 to cancer is likely to reduce benefits associated with MAP vaccination, as some of the infections acquired as MAP may not progress to cancers before persons in the model die of natural causes.

### 4.4 *Other minor differences*

- Both the CDC simplified model and the Merck model use the same input data sources for underlying disease costs, however the CDC simplified model used median costs whereas Merck used mean costs.
- Using mean costs is important from a societal perspective as society must pay all costs incurred, including a small proportion of implausibly large ones. Median costs could arguably be used to

make decisions from an individual perspective. The Second panel for Cost-effectiveness in Health and Medicine recommends use of mean to estimate costs.<sup>70</sup>

- The use of median costs in a societal cost-effectiveness evaluation is not optimal. Given that the vaccine preventable costs are much lower compared to the other costs, the impact of this change is likely to be minimal.

## 5 Cross-validation

A cross-validation exercise<sup>71</sup> across all 3 models could help us assess and resolve the differences in the model results. Some of the parameters that could be evaluated include:

- ICER tables (per-capita) for various scenarios: Per-capita ICER tables, both discounted and undiscounted should be compared across all the models. This will make comparison easier.
- HPV16/18/31/33/45/52/58 prevalence over 100 years with and without MAP vaccination (per 100,000)
- Disease breakdown of all costs and QALYs (per capita)
- Cumulative incidence of HPV infection by age

## 6 Conclusions

- HPV disease is a significant medical concern for MAPs, who continue to acquire new HPV infections that can progress to high-grade disease and cancer.
- Our findings suggest that approximately 50% of CIN2+ cases in the US result from incident HPV infections acquired after the age of 26 years. It is estimated that each year 72,275 - 72,874 cases of CIN2+ attributable to the 7 high risk types in the 9vHPV vaccine arise from infections acquired at age 27 years or older.
- The median age of incident HPV infection of approximately 27 years is also supported by estimates of cumulative HPV infections from the Merck Model, and of annual incident infection obtained from trial/cohort based transmission rates applied to the US population. It is necessary to align the cost-effectiveness modeling on this crucial aspect of HPV infection.
- Sub-groups of MAPs such as persons previously married and not cohabitating, MSM, and MSMW, and online daters are at an even higher risk of acquiring HPV.
- Given that all three models of the cost effectiveness of 9vHPV vaccine in 27-45 year olds have been extensively peer-reviewed and cited, and historically yielded similar cost effectiveness results in younger cohorts, a detailed cross-validation and review of the models is needed to clarify the differences between the models in the MAP population, in order to help decision makers accurately assess the true economic value of HPV vaccination in this age group.

## 7 References

<sup>1</sup> Gardasil 9 Prescribing Information

<sup>2</sup> Chesson H.W., Markowitz L.E., Hariri S., Ekwueme D.U., Saraiya M. The impact and cost-effectiveness of nonavalent HPV vaccination in the United States: Estimates from a simplified transmission model, 2016 Jun 2;12(6):1363-72.

<sup>3</sup> Brisson M., Laprise J.M., Chesson H.W., Drolet M., Malagon T., Boily M.C., Markowitz L.E. Health and Economic Impact of Switching from a 4-Valent to a 9-Valent HPV Vaccination Program in the United States, 2015 Oct 4;108(1). pii: djv282

4 Elbasha E.H., Dasbach E.J. Impact of vaccinating boys and men against HPV in the United States. *Vaccine*. 2010;28(42):6858-67

5 Lewis R., and Markowitz L. Human papillomavirus vaccination coverage among females and males, National Health and Nutrition Examination Survey, United States, 2007–2016. *Vaccine* (2018), <https://doi.org/10.1016/j.vaccine.2018.03.083>

6 Walker T, et al. National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2016. *MMWR*. August 25, 2017, Vol. 66 (33). Pp: 874–882

7 National Survey of Family Growth (NSFG) 2002.

8 Chandra A., Mosher W.D., Copen C., Sionean C. Sexual behavior, sexual attraction, and sexual identity in the United States: data from the 2006–2008 National Survey of Family Growth, 2011 Mar 3;(36):1-36

9 Mosher W.D., Chandra A., Jones J. Sexual behavior and selected health measures: men and women 15–44 years of age, United States, 2002. *Advance data*. 2005(362):1-55

10 Liu, G., Hariri, S., Bradley, H., Gottlieb, S., Leichliter, J., & Markowitz, L. (2015). Trends and Patterns of Sexual Behaviors Among Adolescents and Adults Aged 14 to 59 Years, United States. *Sexually Transmitted Diseases*, 42(1), 20–26. doi: 10.1097/olq.0000000000000231

<sup>11</sup> Mosher W.D., Chandra A., Jones J. Sexual behavior and selected health measures: men and women 15–44 years of age, United States, 2002. *Advance data*. 2005(362):1-55

<sup>12</sup> Liu, G., Hariri, S., Bradley, H., Gottlieb, S., Leichliter, J., & Markowitz, L. (2015). Trends and Patterns of Sexual Behaviors Among Adolescents and Adults Aged 14 to 59 Years, United States. *Sexually Transmitted Diseases*, 42(1), 20–26. doi: 10.1097/olq.0000000000000231

<sup>13</sup> Johnston, L. D., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., Patrick, M. E., & Miech, R. A. (2017). HIV/AIDS: Risk & Protective Behaviors among Adults Ages 21 to 40 in the U.S., 2004–2016. Ann Arbor: Institute for Social Research, The University of Michigan.

<sup>14</sup> Nield, J., Magnusson, B., Chapman, D., & Lapane, K. (2014). Age at Menarche and Risky Sexual Partnerships in Adulthood: Does a Biosocial Model Explain Any Associations?. *Journal Of Women's Health*, 23(4), 342–349. doi: 10.1089/jwh.2013.4S52

<sup>15</sup> Johnston, L. D., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., Patrick, M. E., & Miech, R. A. (2017). HIV/AIDS: Risk & Protective Behaviors among Adults Ages 21 to 40 in the U.S., 2004–2016. Ann Arbor: Institute for Social Research, The University of Michigan.

<sup>16</sup> Darroch J.E., Landry D.J., Oslak S. Age differences between sexual partners in the United States. *Fam Plann Perspect*. 1999;31(4):160-167.

<sup>17</sup> Mosher W.D., Chandra A., Jones J. Sexual behavior and selected health measures: men and women 15–44 years of age, United States, 2002. *Advance data*. 2005(362):1-55

<sup>18</sup> Merck & Co., Inc. Data on file

<sup>19</sup> Sudenga SL, Nyitray AG, Torres BN, Silva R, Villa L, Lazcano-Ponce E, et al. Comparison of anal HPV natural history among men by country of residence: Brazil, Mexico, and the United States. *J Infect*. 2017 Mar 28. [Epub ahead of print].

<sup>20</sup> Winer RL, Hughes JP, JE, Xi LF, Koutsky LA. Incident detection of high-risk Human Papillomavirus infections in a cohort of high-risk women aged 25–65 Years. *J Infect Dis*. 2016 Sep 1;214(5):665-75

- 21 Trottier H, Ferreira S, Thomann P, Costa MC, Sobrinho JS, Prado JC, et al. Human papillomavirus infection and reinfection in adult women: the role of sexual activity and natural immunity. *Cancer Res.* 2010 Nov 1;70(21):8569-77
- 22 Sudenga SL, Nyitray AG, Torres BN, Silva R, Villa L, Lazcano-Ponce E, et al. Comparison of anal HPV natural history among men by country of residence: Brazil, Mexico, and the United States. *J Infect.* 2017 Mar 28. [Epub ahead of print].
- 23 Bautista O, Saah A, Munoz N. Longitudinal study of human papillomavirus persistence and cervical intraepithelial neoplasia grade 2/3: critical role of duration of infection. *J Natl Cancer Inst* 2011; 103:158.
- 24 Skinner, S., Wheeler, C., Romanowski, B., Castellsagué, X., Lazcano-Ponce, E., Rowena Del Rosario-Raymundo, M., Vallejos, C., Minkina, G., Pereira Da Silva, D., McNeil, S., Prilepskaya, V., Gogotadze, I., Money, D., Garland, S., Romanenko, V., Harper, D., Levin, M., Chatterjee, A., Geeraerts, B., Struyf, F., Dubin, G., Bozonnat, M., Rosillon, D. and Baril, L. (2016). Progression of HPV infection to detectable cervical lesions or clearance in adult women: Analysis of the control arm of the VIVIANE study. *International Journal of Cancer*, 138(10), pp.2428-2438.
- 25 Gargano et al. Trends in High-grade Cervical Lesions and Cervical Cancer Screening in 5 States, 2008–2015. *CID* 2018; DOI: 10.1093/cid/ciy707
- 26 Flagg, et al. Population-based surveillance for cervical cancer precursors in three central cancer registries, United States. *CCC* 2014; DOI 10.1007/s10552-014-0362-x.
- 27 Hariri, et al. HPV Type Attribution in High-Grade Cervical Lesions: Assessing the Potential Benefits of Vaccines in a Population-Based Evaluation in the United States. *CEBP* 2014; 24(2):1-7.
- 28 Insinga, et al. Incident Cervical HPV Infections in Young Women: Transition Probabilities for CIN and Infection Clearance. *CEBP* 2011; 20(2):287-296
- 29 Insinga et al. 2011. Incident Cervical HPV Infections in Young Women: Transition Probabilities for CIN and Infection Clearance. *Cancer Epidemiology, Biomarkers, and Prevention*. DOI: 10.1158/1055-9965.EPI-10-0791
- 30 Office of Disease Prevention and Health Promotion. Healthy People 2020: immunization and infectious diseases. <https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives>. Accessed October 18, 2018.
- 31 Merck data on file (details provided in Appendix)
- 32 Garland, et al. Quadrivalent Vaccine against Human Papillomavirus to Prevent High-Grade Cervical Lesions. *N Engl J Med* 2007;356:1915-27.
- 33 Garland, et al. Quadrivalent Vaccine against Human Papillomavirus to Prevent High-Grade Cervical Lesions *N Engl J Med* 2007;356:1928-43.
- 34 Muñoz, et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24–45 years: a randomised, double-blind trial. *Lancet* 2009; 373: 1949–57
- 35 Munoz, N, Mendez F, et al. 2004. Incidence, Duration, and Determinants of Cervical Human Papillomavirus Infection in a Cohort of Colombian Women with Normal Cytological Results *JID* 2004:190
- 36 Arias et al. 2017. United States Life Tables 2014. National Vital Statistics Reports. Vol. 66 {4}
- 37 Burger, et al Age of Acquiring Causal Human Papillomavirus (HPV) Infections: Leveraging Simulation Models to Explore the Natural History of HPV-induced Cervical Cancer. *Clinical Infectious Diseases®* 2017;65(6):893–9
- 38 Chesson H.W., Markowitz L.E., Hariri S., Ekwueme D.U., Saraiya M. The impact and cost-effectiveness of nonavalent HPV vaccination in the United States: Estimates from a simplified transmission model, 2016 Jun 2;12(6):1363-72.
- 39 Brisson M., Laprise J.M., Chesson H.W, Drolet M., Malagon T., Boily M.C., Markowitz L.E. Health and Economic Impact of Switching from a 4-Valent to a 9-Valent HPV Vaccination Program in the United States, 2015 Oct 4;108(1). pii: djv282
- 40 Elbasha E.H., Dasbach E.J. Impact of vaccinating boys and men against HPV in the United States. *Vaccine.* 2010;28(42):6858-67
- 41 <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-feb08-508.pdf>
- 42 <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-oct10.pdf>
- 43 <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-feb11.pdf>
- 44 <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-2015-02.pdf>
- 45 <https://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-2015-06.pdf>



- <sup>46</sup> Elbasha E.H., Dasbach E.J. Impact of vaccinating boys and men against HPV in the United States. *Vaccine*. 2010;28(42):6858-67
- <sup>47</sup> Brisson M., Bénard É., Drolet M. et al. Population-level impact, herd immunity, and elimination after human papillomavirus vaccination: a systematic review and meta-analysis of predictions from transmission-dynamic models. *The Lancet Public Health*. 2016;1.
- <sup>48</sup> Jit M., Demarteau N., Elbasha E. et al. Human papillomavirus vaccine introduction in low-income and middle-income countries: guidance on the use of cost-effectiveness models. *BMC Med*. 2011 May 12;9:54.
- <sup>49</sup> Trottier H, Ferreira S, Thomann P, Costa MC, Sobrinho JS, Prado JC, et al. Human papillomavirus infection and reinfection in adult women: the role of sexual activity and natural immunity. *Cancer Res* 2010;70(21):8569-77
- <sup>50</sup> Fu TC, Carter JJ, Hughes JP, Feng Q, Hawes SE, Schwartz SM, et al. Re-detection vs. new acquisition of high-risk human papillomavirus in mid-adult women. *Int J Cancer* 2016;139(10):2201-12.
- <sup>51</sup> Velicer C, Zhu X, Vuocolo S, Liaw K, Saah,A. 2009. Prevalence and Incidence of HPV Genital Infection in Women. *Sexually Transmitted Diseases*: November 2009 - Volume 36 - Issue 11 - p 696-703
- <sup>52</sup> Elbasha E.H., Dasbach E.J. Impact of vaccinating boys and men against HPV in the United States. *Vaccine*. 2010;28(42):6858-67
- <sup>53</sup> Ho G.Y., Studentsov Y.Y., Bierman R., Burk R.D. Natural history of human papillomavirus type 16 virus-like particle antibodies in young women. *Cancer Epidemiol Biomarkers Prev*. 2004;13(1):110-6;
- <sup>54</sup> Onda T., Carter J.J., Koutsky L.A., Hughes J.P., Lee S.K., Kuypers J. et al. Characterization of IgA response among women with incident HPV 16 infection. *Virology*. 2003;312(1):213-21
- <sup>55</sup> Beachler D.C., Jenkins G., Safaeian M., Kreimer A.R., Wentzensen N. Beach. Natural Acquired Immunity Against Subsequent Genital Human Papillomavirus Infection: A Systematic Review and Meta-analysis. *J Infect Dis*. 2016 May 1;213(9):1444-54.
- <sup>56</sup> Castellsagué, X., Muñoz, N., Pitisuttithum, P., Ferris, D., Monsonego, J., Ault, K., ... Saah, A. (2011). End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24-45 years of age. *British Journal of Cancer*, 105(1), 28-37.
- <sup>57</sup> Olsson SE, Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Wheeler CM, et al. Evaluation of quadrivalent HPV 6/11/16/18 vaccine efficacy against cervical and anogenital disease in subjects with serological evidence of prior vaccine type HPV infection. *Hum Vaccin* 2009;5(10):696-704.
- <sup>58</sup> Castellsagué, X., Muñoz, N., Pitisuttithum, P., Ferris, D., Monsonego, J., Ault, K. et al. (2011). End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24-45 years of age. *British Journal of Cancer*, 105(1), 28-37.
- <sup>59</sup> Canfell K., Barnabas R., Patnick J., Beral V. The predicted effect of changes in cervical screening practice in the UK: results from a modelling study. *Br J Cancer*. 2004;91(3):530-536.
- <sup>60</sup> Barnabas R.V., Garnett G.P. The potential public health impact of vaccines against human papillomavirus. *European Consortium for Cervical Cancer Education*. 2004 (in press)
- <sup>61</sup> Melkert P.W., Hopman E, Van Den Brule A.J., Risse E.K., van Diest P.J., Bleker O.P., Helmerhorst T., Schipper M.E., Meijer C.J., Walboomers J.M. Prevalence of HPV in cytologically normal cervical smears, as determined by the polymerase chain reaction, is age-dependant. *Int J Cancer* 53: 919-923.
- <sup>62</sup> Schiffman M., Kjaer S.K. Chapter 2: Natural history of anogenital human papillomavirus infection and neoplasia. *J Natl Cancer Inst Monogr* 31: 14-19.
- <sup>63</sup> Myers E.R., McCrory D.C., Nanda K., Bastian L., Matchar D.B. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. *Am J Epidemiol*. 2000;151(12):1158-1171.
- <sup>64</sup> Kiviat N. Natural history of cervical neoplasia: overview and update. *Am J Obstet Gynecol* 1996;175:1099-104.
- <sup>65</sup> Ho G.Y.F., Bierman R., Beardsley L. Natural history of cervicovaginal papillomavirus infection in young women. *N Engl J Med* 1998;338:423-8.
- <sup>66</sup> Hildesheim A, Schiffman MH, Gravitt PE, et al. Persistence of type-specific human papillomavirus infection among cytologically normal women. *J Infect Dis* 1994; 169:235-40.
- <sup>67</sup> <http://www.marc-brisson.net/HPVadvise-US.pdf> accessed 10/18/2018
- <sup>68</sup> Darroch J.E., Landry D.J., Oslak S. Age differences between sexual partners in the United States. *Fam Plann Perspect*. 1999;31(4):160-167.



---

<sup>69</sup> Insinga R, et al. Epidemiologic natural history and clinical management of Human Papillomavirus (HPV) Disease: a critical and systematic review of the literature in the development of an HPV dynamic transmission model. *BMC Infectious Diseases* 2009, 9:119

<sup>70</sup> Basu A. Estimating costs and valuations of non-health benefits in cost-effectiveness analysis. From, "Cost-effectiveness in health and medicine." Eds. Neumann P, et al. 2nd Edition, Oxford Univ. Press, New York, NY. 2017

<sup>71</sup> Eddy D, Hollingworth W, Caro J, Tsevat J, McDonald K, Wong J, On Behalf of the ISPOR-SMDM Modeling Good Research Practices Task Force. Model Transparency and Validation. 2012. A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force 7. *Medical Decision making*, Sep.-Oct. 2013. DOI: 10.1177/0272989X12454579

**From:** Grabenstein, John D.  
**Sent:** Wed, 21 Nov 2018 23:49:54 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD)  
**Subject:** Romaine... :-}

Reporting in, oh you public-health leaders!

Our romaine has been consigned to the compost pile. Message cascaded to entire staff.

Wishing you wonderful, relaxing, unplugged, and family-filled Thanksgivings! Ideally, you will receive this message on Monday, but that's doubtful with the faithful such as yourselves.

I promise to cook the turkey to the FDA-recommended (or is it CDC-recommended?) internal temperature with my instant thermometer and to be injury-avoidant during carving!



John

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs  
Merck Research Laboratories  
351 N. Sumneytown Pike, UG-2B09  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** (b)(6)  
**Sent:** Wed, 5 Dec 2018 18:53:03 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Cozart, Barbara (CDC/DDID/NCIRD/OD); (b)(6) Conrad, Patricia (NIH/NIAID)  
[E] (b)(6)  
**Cc:** baltimo@caltech.edu  
**Subject:** 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019  
**Attachments:** AAAS Flu Vaccine Session-Accepted.pdf

You each should have received an email from AAAS requesting abstracts for your individual talks. I had included short abstracts in our original submission from which you can work from -- and have attached these for your convenience (see below for extractions).

Amanda Johnson, communications lead for AAAS, has **Nancy Messonnier, Anthony Fauci and Gary Nabel listed as participating in a news briefing** and she should be coordinating the timing for this directly with you. Gary, Amanda confirmed with John Shiver that he will join you for the briefing.

AAAS is also asking that you **upload your slide presentations by mid-January** since these will be used as a foundation to frame the news briefing.

As a reminder, we will have shorter talks with a panel discussion at the end. For planning, since there is 90 min total for 3 speakers and a short introduction by David Baltimore—this means about 5 min introduction, 20 min for each talk and then 25 min for the panel and Q&A, moderated by David Baltimore. Let me know if you another suggestion.

Wishing you happy holidays.

Best,  
Karen

### **Gary Nabel**

**Title:** Rational Design and Development of Universal Influenza Vaccines

**Summary:** This talk will cover the alternative paths to improved influenza vaccines. Different potential approaches to a broadly protective antibody will be highlighted. Major scientific challenges and opportunities based on influenza biology and the human immune response will be discussed. Finally, considerations for product development will be reviewed, including clinical testing, regulatory, and manufacturing issues, as well as opportunities to advance through public-private partnerships.

### **Anthony Fauci**

**Title:** Chasing Influenza: The Need for a Universal Influenza Vaccine

**Summary:** Strain-specific vaccination for influenza is suboptimal: 1) Seasonal vaccines are not consistently effective 2) Pandemics occur and response after the fact is ineffective 3) chasing after potential pandemic viruses is costly and ineffective. Our goal is a universal influenza vaccine that would protect against both seasonal and pandemic viruses. To achieve this, we must

improve production strategies for influenza vaccines and advance from strain-specific to universal strain coverage.

**Nancy Messonnier**

**Title:** Hit me with your best shot: before and after a universal flu vaccine

**Summary:** While the promise of a universal flu vaccine may be years in the future, how can we reduce flu's burden until one is developed and what ground work can we lay in advance? As we track domestic and international surveillance trends and learn more about how flu works and our response to it, we have to improve our current vaccines and evaluate if different types of vaccine are more beneficial. Data tells us that flu vaccine coverage is linked to how well the vaccine works. Working to ensure the current vaccines are effective and safe before we have a universal vaccine can pave the way for its acceptance.

---

**From:** Chandross, Karen /US

**Sent:** Thursday, November 29, 2018 8:08 AM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; 'Cozart, Barbara (CDC/OID/NCIRD)' <wjn4@cdc.gov>; (b)(6) 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; 'Baltimore, David' <baltimo@caltech.edu>; Nabel, Gary /US

(b)(6) Travayiakis, Carol /US (b)(6) Wei, Ronnie /US

(b)(6)

**Subject:** RE: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

Dear Colleagues,

You may have received an email from AAAS specifying your time slot for our flu session – please let me know if this is not the case.

We are confirmed for Saturday, February 16, 2019 (3:30 – 5 pm) – hoping that you can stay for the entire session.

As a reminder, if you agreed to meet with Amanda Johnson ([abjohnson@aaas.org](mailto:abjohnson@aaas.org)), AAAS' Press Deputy Director, in a press conference to highlight cutting edge science coming out of your research labs before our session, please consider this in your travel plans. As previously mentioned, I had suggested a group interview (if feasible) around ways of working together to solve some of the biggest challenges to achieving broadly protective or universal vaccines. I will follow up around where this stands.

I'll reach out again with any updates before the winter holidays.

Best regards,  
Karen

---

**From:** Chandross, Karen /US

**Sent:** Monday, October 1, 2018 1:28 PM

To: 'Messonnier, Nancy (CDC/OID/NCIRD)' <[nar5@cdc.gov](mailto:nar5@cdc.gov)>; 'Cozart, Barbara (CDC/OID/NCIRD)' <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>; (b)(6); 'Conrad, Patricia (NIH/NIAID) [E]' <[conradpa@niaid.nih.gov](mailto:conradpa@niaid.nih.gov)>; 'Baltimore, David' <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; Nabel, Gary /US (b)(6); Travayiakis, Carol /US <(b)(6)> Wei, Ronnie /US (b)(6)

**Subject:** FW: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

Dear Colleagues,

Our **flu vaccine session is confirmed for Saturday, February 16, 2019 (3:30 – 5 pm)** – if you would be please block your calendars, register for the meeting and finalize your travel arrangements as soon as possible.

You should have received the registration link (which then also opens up hotel registration) directly from the AAAS. If this is not the case, please reach out to Ashira Greene ([agreene@aaas.org](mailto:agreene@aaas.org)) directly.

You may have been contacted by Amanda Johnson, AAAS' Press Deputy Director. She would like to highlight cutting edge science coming out of your research labs in a press conference, to be held before our session – so please consider this when planning your travel. I had suggested that since this session involves very senior level experts from across the different healthcare sectors, it could be interesting to engage the panel (together) around ways of working together to solve some of the biggest challenges to achieving broadly protective or universal vaccines.

Thank you.  
Karen

**From:** [aaas@confex.com](mailto:aaas@confex.com) [<mailto:aaas@confex.com>]  
**Sent:** Monday, October 1, 2018 11:58 AM  
**To:** Chandross, Karen /US (b)(6)  
**Subject:** [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule



Dear Karen Chandross, PhD,

Your session at the 2019 AAAS Annual Meeting in Washington, DC has been scheduled.

Title: The Quest for a Universal Flu Vaccine  
Date: Saturday, February 16, 2019  
Time: 3:30 PM to 5:00 PM

Scheduling took many variables into consideration, including speaker and organizer conflicts. The schedule is final and additional changes are unable

to be accommodated. If an emergency arises, please contact me. If you are organizing more than one session, you will receive a separate email for each one.

Please inform the participants in your session(s). Organizers are responsible to disseminate this and other relevant information to all participants in their panels.

The room will be equipped with an LCD projector and screen, a laptop, a head table for three, one podium microphone, and one table microphone, which will be billed to AAAS. Shared Wi-Fi will be available in the meeting rooms. The addition of extra equipment, such as a wired Internet connection, presentation remote, or additional microphones is your responsibility and will not be billed to AAAS. To order additional equipment at your cost, a list of vendors will be available on your [Participant Page](#) in late January. This [page](#) will be updated several times before February with logistical information, tools, and tips for your use in preparing your presentation.

Starting in late December, AAAS will poll registrants as to which sessions they are most interested in attending. Once the results are in, the room assignments will be determined and published in late January. Poll results will strongly affect but not be the only determining factor in room assignments.

For more information about the 2019 AAAS Annual Meeting, visit [www.aaas.org/meetings](http://www.aaas.org/meetings). The meeting schedule will be available online Tuesday, October 9, 2018. Meeting registration is open; all confirmed speakers have received registration instructions by email. If you have questions about how to register, please email [meetings@aaas.org](mailto:meetings@aaas.org).

If you must withdraw your session, make a presenter change, or have questions about your session, please contact me as soon as possible at [agreene@aaas.org](mailto:agreene@aaas.org) or (202) 326-6593.

Sincerely,  
Ashira

**Ashira B. Greene, Ph.D.**

Program Associate, Office of Meetings and Special Events  
American Association for the Advancement of Science  
1200 New York Avenue NW  
Washington, DC 20005  
P: 202-326-6593  
E: [agreene@aaas.org](mailto:agreene@aaas.org)

**AAAS Annual Meeting**

February 14-17, 2019 • Washington, DC

[www.aaas.org/meetings](http://www.aaas.org/meetings)



**From:** (b)(6)  
**Sent:** Thu, 6 Sep 2018 15:07:45 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD); Cozart, Barbara (CDC/OID/NCIRD); (b)(6) Conrad, Patricia (NIH/NIAID) [E]; baltimo@caltech.edu (b)(6)  
**Subject:** RE: AAAS 2019 Annual Meeting: Travel Support Request Information & Flu session update

Dear Colleagues,

As an update, if you wish to apply for travel support, please see the link below—with a deadline of Sept 27<sup>th</sup>.

For our “Universal Flu” session, we have the 90 min symposium format, with 3 speakers. I received permission from the organizers to incorporate a panel discussion into this session, where we can come prepared with topics but also engage the audience. This would mean shorter talks by each speaker (20 min) followed by the panel discussion (30 min) moderated by David Baltimore. Please let me know whether this session format is agreeable to you.

Thank you.  
Karen

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL: (b)(6) (b)(6)

**From:** aaas@confex.com [mailto:aaas@confex.com]  
**Sent:** Thursday, September 6, 2018 9:41 AM  
**To:** Chandross, Karen /US <(b)(6)>  
**Subject:** [EXTERNAL] AAAS 2019 Annual Meeting: Travel Support Request Information



**\* Deadline for panelists to apply for travel support: Thursday, September 27 at 11:59 p.m. PT.\***

\*\*\*\*\*

**Instructions for Speakers – Travel Support Request**

2019 AAAS Annual Meeting speakers interested in applying for travel support must do so by September 27, 2018 at 11:59 p.m. PT. All requests must be submitted online through the AAAS Travel Support Request website: <https://annualmeeting.aaas.org/>.

To submit a travel support request, a speaker must create an account online and follow the instructions. Please note that applying for travel support is not a guarantee that funding will be awarded. The disciplinary sections of AAAS may choose to authorize travel support from their modest budgets. Speakers will be notified of the decision regarding their request in early November.

\*\*\*\*\*

If you have any questions, please email [meetings@aaas.org](mailto:meetings@aaas.org) or call (202) 326-6450.

AAAS Meetings Staff  
1200 New York Avenue NW  
Washington, DC 20005  
Phone: (202) 326-6450  
Email: [meetings@aaas.org](mailto:meetings@aaas.org)

**AAAS Annual Meeting**  
February 14-17, 2019 • Washington, DC  
[www.aaas.org/meetings](http://www.aaas.org/meetings)

**From:** (b)(6)  
**Sent:** Tue, 4 Sep 2018 10:56:17 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD); Cozart, Barbara (CDC/OID/NCIRD); (b)(6); Conrad, Patricia (NIH/NIAID) [E]; baltimo@caltech.edu (b)(6)  
**Cc:** (b)(6)  
**Subject:** FW: [EXTERNAL] AAAS 2019 Annual Meeting Confirmation of Participation -- Confirming receipt

Dear Colleagues,

I'm reaching out to make sure that you received an email similar to the one below – used to verify your participation. You should also have been given a username and password.

If not, please let me know and I'll follow-up with the AAAS organizers.

Thank you.  
Karen

**From:** aaas@confex.com [mailto:aaas@confex.com]  
**Sent:** Thursday, August 30, 2018 2:47 PM  
**To:** Chandross, Karen /US (b)(6)  
**Subject:** [EXTERNAL] AAAS 2019 Annual Meeting Confirmation of Participation



Dear Karen Chandross, PhD:

As you know, your scientific session, 21433 "The Quest for a Universal Flu Vaccine," has been accepted by the Program Committee for the 2019 AAAS Annual Meeting, to be held February 14-17 in Washington, DC. You are listed as a session Organizer.

Please click the link below to confirm participation by September 14. If you are involved with more than one session, you will receive a separate e-mail for each one.

[https://aaas.confex.com/aaas/2019/speakerscorner.cgi?username=\(b\)\(6\)&password=\(b\)\(6\)17&EntryType=Person](https://aaas.confex.com/aaas/2019/speakerscorner.cgi?username=(b)(6)&password=(b)(6)17&EntryType=Person)

If you are asked to enter a username and password, please use the following:

Username: (b)(6)  
Password: (b)(6)

As a reminder, here is what to expect in the coming months:

- **Early August:** All participants will receive information about registration and housing when these sites open online. Information about applying for travel support will be sent only to you (the organizer), with further instructions for informing your panelists. **To register with the reduced rate, participants must use the link that will be emailed to them from Experient, the AAAS registration service provider.**
- **Late September:** Session organizers will receive information about their session's date and time assignment.
- **Early October:** The meeting program and schedule will be posted online, without room assignments.
- **November:** Speakers are requested to provide updated lay-language summaries of their talks and other background, for use in encouraging media coverage of your session.
- **Early January:** Current registrants will be asked to indicate the sessions they are most interested. This feedback will help guide room assignments.

If you have questions about the Annual Meeting, please reply to this e-mail or call (202) 326-6593.

Sincerely,

Ashira B. Greene

Program Associate

### **AAAS Annual Meeting**

February 14-17, 2019 • Washington, DC

[www.aaas.org/meetings](http://www.aaas.org/meetings)



**From:** (b)(6)  
**Sent:** Tue, 8 Jan 2019 18:12:30 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Cozart, Barbara (CDC/DDID/NCIRD/OD) (b)(6) Conrad, Patricia (NIH/NIAID) [E] (b)(6)  
**Cc:** baltimo@caltech.edu  
**Subject:** 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019 - Please submit materials

Wishing you all a very Happy New Year!

For our flu session, by now you should be uploading any materials you would like shared at our Feb 16<sup>th</sup> press briefing and finalizing your presentations. You should also send materials to me as a backup and I'll be sure they are added to flu session account.

As a reminder -- Drs. Nabel, Messonnier and Fauci -- please plan for a 20 min talk to include 5 min for Q&A. Your talks will be followed by a panel discussion led by Dr. Baltimore. We are working on the panel topics and will share these in the coming weeks.

Please let me know if you have any questions.

Thank you.  
Karen

**From:** Chandross, Karen /US  
**Sent:** Wednesday, December 5, 2018 1:53 PM  
**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; 'Cozart, Barbara (CDC/OID/NCIRD)' <wjn4@cdc.gov>; (b)(6) 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; Nabel, Gary /US <(b)(6)>; Travayiakis, Carol /US <(b)(6)>; Wei, Ronnie /US <(b)(6)>  
**Cc:** 'Baltimore, David' <baltimo@caltech.edu>  
**Subject:** RE: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

You each should have received an email from AAAS requesting abstracts for your individual talks. I had included short abstracts in our original submission from which you can work from -- and have attached these for your convenience (see below for extractions).

Amanda Johnson, communications lead for AAAS, has **Nancy Messonnier, Anthony Fauci and Gary Nabel listed as participating in a news briefing** and she should be coordinating the timing for this directly with you. Gary, Amanda confirmed with John Shiver that he will join you for the briefing.

AAAS is also asking that you **upload your slide presentations by mid-January** since these will be used as a foundation to frame the news briefing.

As a reminder, we will have shorter talks with a panel discussion at the end. For planning, since there is 90 min total for 3 speakers and a short introduction by David Baltimore--this means about 5 min

introduction, 20 min for each talk and then 25 min for the panel and Q&A, moderated by David Baltimore. Let me know if you another suggestion.

Wishing you happy holidays.

Best,  
Karen

### **Gary Nabel**

**Title:** Rational Design and Development of Universal Influenza Vaccines

**Summary:** This talk will cover the alternative paths to improved influenza vaccines. Different potential approaches to a broadly protective antibody will be highlighted. Major scientific challenges and opportunities based on influenza biology and the human immune response will be discussed. Finally, considerations for product development will be reviewed, including clinical testing, regulatory, and manufacturing issues, as well as opportunities to advance through public-private partnerships.

### **Anthony Fauci**

**Title:** Chasing Influenza: The Need for a Universal Influenza Vaccine

**Summary:** Strain-specific vaccination for influenza is suboptimal: 1) Seasonal vaccines are not consistently effective 2) Pandemics occur and response after the fact is ineffective 3) chasing after potential pandemic viruses is costly and ineffective. Our goal is a universal influenza vaccine that would protect against both seasonal and pandemic viruses. To achieve this, we must improve production strategies for influenza vaccines and advance from strain-specific to universal strain coverage.

### **Nancy Messonnier**

**Title:** Hit me with your best shot: before and after a universal flu vaccine

**Summary:** While the promise of a universal flu vaccine may be years in the future, how can we reduce flu's burden until one is developed and what ground work can we lay in advance? As we track domestic and international surveillance trends and learn more about how flu works and our response to it, we have to improve our current vaccines and evaluate if different types of vaccine are more beneficial. Data tells us that flu vaccine coverage is linked to how well the vaccine works. Working to ensure the current vaccines are effective and safe before we have a universal vaccine can pave the way for its acceptance.

---

**From:** Chandross, Karen /US

**Sent:** Thursday, November 29, 2018 8:08 AM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <[nar5@cdc.gov](mailto:nar5@cdc.gov)>; 'Cozart, Barbara (CDC/OID/NCIRD)' <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>; (b)(6); 'Conrad, Patricia (NIH/NIAID) [E]' <[conradpa@niaid.nih.gov](mailto:conradpa@niaid.nih.gov)>; 'Baltimore, David' <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; Nabel, Gary /US

(b)(6); Travayiakis, Carol /US (b)(6); Wei, Ronnie /US

(b)(6)

**Subject:** RE: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

Dear Colleagues,

You may have received an email from AAAS specifying your time slot for our flu session – please let me know if this is not the case.

We are confirmed for Saturday, February 16, 2019 (3:30 – 5 pm) – hoping that you can stay for the entire session.

As a reminder, if you agreed to meet with Amanda Johnson ([abjohnson@aaas.org](mailto:abjohnson@aaas.org)), AAAS' Press Deputy Director, in a press conference to highlight cutting edge science coming out of your research labs before our session, please consider this in your travel plans. As previously mentioned, I had suggested a group interview (if feasible) around ways of working together to solve some of the biggest challenges to achieving broadly protective or universal vaccines. I will follow up around where this stands.

I'll reach out again with any updates before the winter holidays.

Best regards,  
Karen

**From:** Chandross, Karen /US

**Sent:** Monday, October 1, 2018 1:28 PM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <[nar5@cdc.gov](mailto:nar5@cdc.gov)>; 'Cozart, Barbara (CDC/OID/NCIRD)' <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>; (b)(6); 'Conrad, Patricia (NIH/NIAID) [E]' <[conradpa@niaid.nih.gov](mailto:conradpa@niaid.nih.gov)>; 'Baltimore, David' <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; Nabel, Gary /US

(b)(6)

Travayiakis, Carol /US (b)(6) Wei, Ronnie /US

(b)(6)

**Subject:** FW: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

Dear Colleagues,

Our **flu vaccine session is confirmed for Saturday, February 16, 2019 (3:30 – 5 pm)** – if you would be please block your calendars, register for the meeting and finalize your travel arrangements as soon as possible.

You should have received the registration link (which then also opens up hotel registration) directly from the AAAS. If this is not the case, please reach out to Ashira Greene ([agreene@aaas.org](mailto:agreene@aaas.org)) directly.

You may have been contacted by Amanda Johnson, AAAS' Press Deputy Director. She would like to highlight cutting edge science coming out of your research labs in a press conference, to be held before our session – so please consider this when planning your travel. I had suggested that since this session involves very senior level experts from across the different healthcare sectors, it could be interesting to engage the panel (together) around ways of working together to solve some of the biggest challenges to achieving broadly protective or universal vaccines.



Thank you.  
Karen

**From:** [aaas@confex.com](mailto:aaas@confex.com) [<mailto:aaas@confex.com>]  
**Sent:** Monday, October 1, 2018 11:58 AM  
**To:** Chandross, Karen /US (b)(6)  
**Subject:** [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule



Dear Karen Chandross, PhD,

Your session at the 2019 AAAS Annual Meeting in Washington, DC has been scheduled.

Title: The Quest for a Universal Flu Vaccine  
Date: Saturday, February 16, 2019  
Time: 3:30 PM to 5:00 PM

Scheduling took many variables into consideration, including speaker and organizer conflicts. The schedule is final and additional changes are unable to be accommodated. If an emergency arises, please contact me. If you are organizing more than one session, you will receive a separate email for each one.

Please inform the participants in your session(s). Organizers are responsible to disseminate this and other relevant information to all participants in their panels.

The room will be equipped with an LCD projector and screen, a laptop, a head table for three, one podium microphone, and one table microphone, which will be billed to AAAS. Shared Wi-Fi will be available in the meeting rooms. The addition of extra equipment, such as a wired Internet connection, presentation remote, or additional microphones is your responsibility and will not be billed to AAAS. To order additional equipment at your cost, a list of vendors will be available on your [Participant Page](#) in late January. This [page](#) will be updated several times before February with logistical information, tools, and tips for your use in preparing your presentation.

Starting in late December, AAAS will poll registrants as to which sessions they are most interested in attending. Once the results are in, the room

assignments will be determined and published in late January. Poll results will strongly affect but not be the only determining factor in room assignments.

For more information about the 2019 AAAS Annual Meeting, visit [www.aaas.org/meetings](http://www.aaas.org/meetings). The meeting schedule will be available online Tuesday, October 9, 2018. Meeting registration is open; all confirmed speakers have received registration instructions by email. If you have questions about how to register, please email [meetings@aaas.org](mailto:meetings@aaas.org).

If you must withdraw your session, make a presenter change, or have questions about your session, please contact me as soon as possible at [agreene@aaas.org](mailto:agreene@aaas.org) or (202) 326-6593.

Sincerely,  
Ashira

**Ashira B. Greene, Ph.D.**

Program Associate, Office of Meetings and Special Events  
American Association for the Advancement of Science  
1200 New York Avenue NW  
Washington, DC 20005  
P: 202-326-6593  
E: [agreene@aaas.org](mailto:agreene@aaas.org)

**AAAS Annual Meeting**

February 14-17, 2019 • Washington, DC  
[www.aaas.org/meetings](http://www.aaas.org/meetings)

**From:** (b)(6)  
**Sent:** Fri, 15 Feb 2019 22:19:33 +0000  
**To:** Messonnier, Nancy  
(CDC/DDID/NCIRD/OD); (b)(6); baltimo@caltech.edu  
**Cc:** Cozart, Barbara (CDC/DDID/NCIRD/OD); Conrad, Patricia (NIH/NIAID)  
[E]; (b)(6); ktclark@caltech.edu; Connelly, Erin (CDC/DDID/NCIRD/OD); Marston, Hilary (NIH/NIAID) [E]; (b)(6)  
**Subject:** RE: 2019 AAAS Annual Meeting -- Flu Session Feb 16, 2019 -- final comments before tomorrow

Anticipating that you may wish to make minor revisions to your presentations, when you get to the Marriott Wardman Park hotel, please go to registration desk (on your left once inside the main entrance) to register/pick up your badge and then you can go to the Speaker Ready Room, in McKinley (up the escalators), any time before 3 pm and provide them with your slide deck. You can tell them that this is for the session entitled, "The Quest for a Universal Flu Vaccine," in the "Maryland suite" at 3:30 pm.

We can touch base tomorrow morning at the news briefing - and I'll be ready to put any updated versions onto my memory stick for the organizers, if this is preferred.

Thank you.

Karen

(b)(6) cell)

**Karen CHANDROSS, PhD**

Sr. Director, Sanofi R&D

TEL: (b)(6) | CELL: (b)(6) (b)(6)

**From:** Chandross, Karen /US

**Sent:** Thursday, February 7, 2019 2:59 PM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; (b)(6)  
(b)(6); Nabel, Gary /US (b)(6) 'Baltimore, David' <baltimo@caltech.edu>

**Cc:** 'Cozart, Barbara (CDC/OID/NCIRD)' <wjn4@cdc.gov>; 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; Travayiakis, Carol /US <(b)(6)>; 'Clark, Katie' <ktclark@caltech.edu>; Connelly, Erin (CDC/DDID/NCIRD/OD) <efd5@cdc.gov>; 'Marston, Hilary (NIH/NIAID) [E]' <hilary.marston@nih.gov>

**Subject:** RE: 2019 AAAS Annual Meeting -- Flu Session Feb 16, 2019

Dear Colleagues,

Here is the link to our Feb 16<sup>th</sup> afternoon session:

<https://aaas.confex.com/aaas/2019/meetingapp.cgi/Session/21433> .

It will be held at the Marriott Wardman Park, in the Maryland Suite.

If you would like to send me your presentations, then I'll have these available on a memory stick as backup.

Let me know if you have any final questions and feel free to reach me on my cell at:

(b)(6)

I'll be arriving late afternoon of Feb 15<sup>th</sup> and will make myself available.

I would like to thank you and those copied for your support in the preparations.

Looking forward to an exciting interaction and to meeting you in person!!

Best,  
Karen

**Karen CHANDROSS, PhD**

Sr. Director  
Sanofi R&D

TEL

(b)(6)

CELL:

(b)(6)

(b)(6)

**From:** (b)(6)  
**Sent:** Tue, 26 Feb 2019 13:25:53 +0000  
**To:** Messonnier, Nancy  
(CDC/DDID/NCIRD/OD); (b)(6); baltimo@caltech.edu  
**Cc:** Cozart, Barbara (CDC/DDID/NCIRD/OD); Conrad, Patricia (NIH/NIAID)  
[E]; (b)(6) ktclark@caltech.edu; Connelly, Erin (CDC/DDID/NCIRD/OD); Marston,  
Hilary (NIH/NIAID) [E]  
**Subject:** RE: 2019 AAAS Annual Meeting -- Feb 16th Flu Session -- Thank you  
**Attachments:** IMG\_0378.jpg, IMG\_0379.jpg, IMG\_0381.jpg, IMG\_0386.jpg, IMG\_0390.jpg,  
IMG\_0398.jpg

A quick note to thank you for your participation in our AAAS session, The Quest for a Universal Flu Vaccine!

Attached are a few photos. Check out Nancy's badge!

Wishing you all the best,  
Karen

**Karen CHANDROSS, PhD**

Senior Director  
Sanofi R&D

TEL: (b)(6) | CELL: (b)(6) | (b)(6)

(b)(6)

(b)(6)



(b)(6)

(b)(6)

(b)(6)

(b)(6)

**From:** Leonard Friedland  
**Sent:** Mon, 11 Mar 2019 16:30:20 +0000  
**To:** Cohn, Amanda (CDC/DDID/NCIRD/OD); Messonnier, Nancy (CDC/DDID/NCIRD/OD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)  
**Subject:** RE: GSK Vaccines - early vaccine in development topic to discuss

Dear Amanda, Nancy and Jessica,

I was not able to speak with you at the ACIP meeting.

Please see the message below (b)(4)

(b)(4) I'd like to discuss setting up time in Q3 to discuss the development program.

Best regards, Len

---

**From:** Leonard Friedland  
**Sent:** Wednesday, February 20, 2019 5:05 PM  
**To:** Amanda Cohn <anc0@cdc.gov>; Nancy Messonnier (nar5@cdc.gov) <nar5@cdc.gov>; jmacneil@cdc.gov  
**Subject:** GSK Vaccines - early vaccine in development topic to discuss

Dear Amanda, Nancy and Jessica,

I was planning to sidebar you at the Feb ACIP meeting to mention the following; though not sure there will be opportunity at the meeting.

(b)(4)

Best regards, Len

Leonard Friedland, MD  
VP, Scientific Affairs and Public Health  
GSK Vaccines

(b)(6)

**GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.**

**From:** Coen, Lisa  
**Sent:** Fri, 13 Sep 2019 13:00:51 +0000  
**To:** Cohn, Amanda (CDC/DDID/NCIRD/OD); Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Aleshire, Noah (CDC/DDID/NCIRD/OD); Snow, Vincenza T; Cane, Alejandro  
**Subject:** Introductory meeting request

Dear Dr. Messonnier and Dr. Cohn – I am writing on behalf of our senior leaders, Dave Hering (North America President for Pfizer Vaccines) and Alejandro Cane (Vice President, Medical Affairs), to seek an in person meeting with you. In recent months, we have made several changes across our Pfizer vaccines team and would be grateful for the chance to meet, introduce our team, and outline our responsibilities in working with you and your team members.

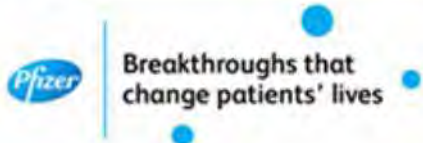
As for timing, we were hoping to meet ahead of the October 1<sup>st</sup> meeting at BIO that we understand you'll both attend, but would want to defer to your schedule. We could meet with you at CDC in Atlanta or in Washington, DC, if that's more convenient.

Thank you for your consideration of this request. We're looking forward to meeting with you.

Kind regards,  
Lisa

---

**Lisa Coen**  
U.S. Public Affairs Lead | Pfizer Vaccines  
1275 Pennsylvania Ave. NW #600 | Washington, DC 20004  
Mobile: [REDACTED]  
Email: [REDACTED]





**From:** Kuter, Barbara J.  
**Sent:** Thu, 24 Oct 2019 03:52:52 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** Markowitz, Lauri (CDC/DDID/NCIRD/DVD); Haupt, Richard M  
**Subject:** HPV - SAGE Minutes

Hi Nancy,

This note is in followup to our discussion today at ACIP. As requested, I am sending along the link to the minutes from the October SAGE meeting. The HPV section starts on page 3.

[https://www.who.int/immunization/sage/meetings/2019/october/SAGE\\_Oct\\_2019\\_Meeting\\_Highlights.pdf?ua=1](https://www.who.int/immunization/sage/meetings/2019/october/SAGE_Oct_2019_Meeting_Highlights.pdf?ua=1)

The minutes state that in the context of limited HPV vaccine supply, SAGE recommends that all countries should temporarily postpone implementation of HPV vaccination strategies that are gender neutral as well as vaccination of older age groups (>15 years) and multi-age cohorts. From the discussion at the meeting, it was our understanding that the suspension applied to new gender neutral programs only, not existing programs. You may want to seek further clarification on this from WHO.

Barb

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Villar, Carmen Sachiko  
**Sent:** Thu, 31 Jan 2019 21:28:48 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** Spencer, Julia  
**Subject:** thank you!

Dear Nancy:

On behalf of the Merck team, I wanted to thank you and the team for meeting with us last week to discuss the global HPV and cervical cancer agenda. It was really helpful for us to hear more about CDC's connections to this work across the global immunization, cancer, and HIV offices, and to have an chance to provide an overview of our engagement in the discussions surrounding WHO's 2018 Call to Action. We also appreciated the opportunity for a transparent dialogue on our global HPV vaccine manufacturing supply plans and our commitment to increasing global HPV vaccine supply. We came away from the meeting feeling very aligned on the opportunities and challenges in addressing HPV cancers and diseases globally.

We look forward to continuing this dialogue as the broader global agenda takes shape in 2019 and 2020. I will follow up directly to schedule a call on the items we discussed at the end of the meeting and Julia will connect with Noah on the broader set of next steps that the group identified.

Take care and look forward to staying in touch!  
Carmen

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Jodar, Luis  
**Sent:** Mon, 25 Feb 2019 17:33:31 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** FW: PCV13 CE technical report and slides

Dear Nancy- I hope all is well. Please find below a message to the CDC that we have just sent (b)(4)  
(b)(4) I am sure that you will eventually get this but I wanted to give you a heads up.

(b)(4)

At this point, if you find it appropriate I think it may be worthwhile to have a short discussion around the note below between you and me. We can do this either face to face or by phone. It is always preferable to meet face to face but given how busy you and your group will be for the upcoming ACIP I would not like to impose.

In any case, I am arriving to Atlanta on Tuesday February 26, at 5.30 pm. I am at your disposal at any time until the pneumococcal discussion on Thursday morning.

I am looking forward to hearing from you,  
Luis

---

**From:** Isturiz, Raul  
**Sent:** Monday, February 25, 2019 9:52 AM  
**To:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD)  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD); Mahon, Barbara (CDC/DDID/NCIRD/DBD); Jodar, Luis; Cohn, Amanda (CDC/DDID/NCIRD/OD)  
**Subject:** RE: PCV13 CE technical report and slides

Thanks very much Almea.

(b)(4)

(b)(4)

(b)(4)

Thanks very much for your attention to the above, we are looking forward to hearing from you and as always remain at your disposal,

Raul

---

**From:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) [mailto:xdf2@cdc.gov]

**Sent:** Friday, February 22, 2019 2:09 PM

**To:** Isturiz, Raul

**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD); Mahon, Barbara (CDC/DDID/NCIRD/DBD); Jodar, Luis; Craig, Allen (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD); gmlee@stanford.edu

**Subject:** [EXTERNAL] RE: PCV13 CE technical report and slides

Dear Raul,

Yes, that is correct. Charles Stoecker's model uses the following parameters for ST3 VE:

| Vaccine Effectiveness |               |      |         |
|-----------------------|---------------|------|---------|
|                       | Disease       | base | range   |
| PCV13                 | ST3 IPD       | 0    | (0, 26) |
| PCV13                 | ST3 pneumonia | 0    | (0, 45) |

Thank you,  
Almea

---

**From:** Isturiz, Raul <(b)(6)>

**Sent:** Friday, February 22, 2019 1:54 PM

**To:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) <xdf2@cdc.gov>

**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD) <tdp4@cdc.gov>; Mahon, Barbara

(CDC/DDID/NCIRD/DBD) <bdm3@cdc.gov>; Jodar, Luis (b)(6); Craig, Allen (CDC/DDID/NCIRD/OD) <afc0@cdc.gov>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>; gmlee@stanford.edu  
**Subject:** RE: PCV13 CE technical report and slides

Hi Almea, we have been giving these a lot of consideration.

Can you confirm that the base case VE against serotype 3 in the Charles Stoecker CE model remains 0%?

Many thanks for your prompt attention to this important question.

Best,

Raul

---

**From:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) [<mailto:xdf2@cdc.gov>]  
**Sent:** Friday, February 15, 2019 4:07 PM  
**To:** Isturiz, Raul  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD); Mahon, Barbara (CDC/DDID/NCIRD/DBD); Jodar, Luis; Craig, Allen (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD); [gmlee@stanford.edu](mailto:gmlee@stanford.edu)  
**Subject:** [EXTERNAL] RE: PCV13 CE technical report and slides

Dear Raul,

Thank you for this information and the responses to our questions you have sent as well. We will review and get back to you with any questions in the next few days. We will most definitely share the information that is relevant to the current policy question with the workgroup.

The assumptions for VE in Charles' model are unchanged with the exception of the PCV13 VE against VT-pneumonia (non-bacteremic) for health adults—now 63.8% (14.7–86.1) from Suaya et al. Charles is not presenting at ACIP again and so there is no comprehensive report to share. The updated model results will be shown in the CDC health economics team's side-by-side comparison presentation.

Thank you again,  
Almea

---

**From:** Isturiz, Raul (b)(6)  
**Sent:** Thursday, February 14, 2019 9:17 AM  
**To:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) <[xdf2@cdc.gov](mailto:xdf2@cdc.gov)>  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD) <[tdp4@cdc.gov](mailto:tdp4@cdc.gov)>; Mahon, Barbara (CDC/DDID/NCIRD/DBD) <[bdm3@cdc.gov](mailto:bdm3@cdc.gov)>; Jodar, Luis (b)(6); Craig, Allen (CDC/DDID/NCIRD/OD) <[afc0@cdc.gov](mailto:afc0@cdc.gov)>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <[anc0@cdc.gov](mailto:anc0@cdc.gov)>; [gmlee@stanford.edu](mailto:gmlee@stanford.edu)  
**Subject:** RE: PCV13 CE technical report and slides

Thanks Almea, I have distributed your note appropriately and we will do our best to meet the deadline.



We would like to ask if the CAPiTA VE in risk groups, or any other updates, were also addressed in the revised analysis? Will we have an opportunity to see the revised analysis prior to the ACIP meeting?

Attached, as requested, please find a short presentation (just 3 slides) summarizing PCV13 adult recommendations around the world, slide (1) is an updated summary. I also include an idea of the timelines for recommendations (2) and reimbursement (3). I have a very large presentation I can share if you need it.

I shall be sending answers to all your most recent questions before eob today, doing final checks and QC with John and Qin.

Again, thanks for you flexibility and diligence.

Raul

---

**From:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) [<mailto:xdf2@cdc.gov>]

**Sent:** Wednesday, February 13, 2019 6:30 PM

**To:** Isturiz, Raul

**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD); Mahon, Barbara (CDC/DDID/NCIRD/DBD); Jodar, Luis; Craig, Allen (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD); [gmlee@stanford.edu](mailto:gmlee@stanford.edu)

**Subject:** [EXTERNAL] RE: PCV13 CE technical report and slides

Dear Raul,

Please thank Reiko for the presentation Monday. Attached is the CDC economic review of the most recent model submitted. Please let me know if you have any questions about the attached. If you could please address the comments in this review by the end of 2/19.

For your information, the CFRs for pneumonia in the Stoecker model have been updated as follows:

**Pneumonia CFR**

| Age group | Point estimate (%) | LB (%) | UB (%) |
|-----------|--------------------|--------|--------|
| 65-74     | 3.70               | 1.30   | 6.10   |
| 75-84     | 4.71               | 2.06   | 7.37   |
| 85+       | 7.17               | 4.91   | 9.43   |

Source: NIS 2014, CFR for inpatient pneumonia based on 2013-2014 data

Approach:

- Point estimate: mean of lower and upper bounds
- Lower bound: use ICD-9=481 as principle location
- Upper bound: use ICD-9=481 in any location



Additionally, on the call on Monday, Brad mentioned a number of countries where PCV13 is recommended for adults. Do you have a list of the countries that have national recommendations for universal PCV13 use among older adults? If so, we would appreciate this information to ensure we are interpreting other countries' findings correctly.

Thank you,  
Almea

---

**From:** Isturiz, Raul <(b)(6)>  
**Sent:** Tuesday, February 5, 2019 4:22 PM  
**To:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) <[xdf2@cdc.gov](mailto:xdf2@cdc.gov)>  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD) <[tdp4@cdc.gov](mailto:tdp4@cdc.gov)>; Mahon, Barbara (CDC/DDID/NCIRD/DBD) <[bdm3@cdc.gov](mailto:bdm3@cdc.gov)>; Jodar, Luis <(b)(6)>; Craig, Allen (CDC/DDID/NCIRD/OD) <[afc0@cdc.gov](mailto:afc0@cdc.gov)>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <[anc0@cdc.gov](mailto:anc0@cdc.gov)>; [gmllee@stanford.edu](mailto:gmllee@stanford.edu)  
**Subject:** RE: PCV13 CE technical report and slides

No problem, resending.

Raul

---

**From:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) [<mailto:xdf2@cdc.gov>]  
**Sent:** Tuesday, February 5, 2019 3:52 PM  
**To:** Isturiz, Raul  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD); Mahon, Barbara (CDC/DDID/NCIRD/DBD); Jodar, Luis; Craig, Allen (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD); [gmllee@stanford.edu](mailto:gmllee@stanford.edu)  
**Subject:** [EXTERNAL] RE: PCV13 CE technical report and slides

Dear Raul,  
Apologies if there is something I missed, but I think Appendix A and B are missing and that Appendix C is labeled as A. Could you possibly double check these and resend?  
Thank you again,  
Almea

---

**From:** Isturiz, Raul <(b)(6)>  
**Sent:** Friday, February 1, 2019 2:43 PM  
**To:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) <[xdf2@cdc.gov](mailto:xdf2@cdc.gov)>  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD) <[tdp4@cdc.gov](mailto:tdp4@cdc.gov)>; Mahon, Barbara (CDC/DDID/NCIRD/DBD) <[bdm3@cdc.gov](mailto:bdm3@cdc.gov)>; Jodar, Luis <(b)(6)>; Craig, Allen (CDC/DDID/NCIRD/OD) <[afc0@cdc.gov](mailto:afc0@cdc.gov)>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <[anc0@cdc.gov](mailto:anc0@cdc.gov)>; [gmllee@stanford.edu](mailto:gmllee@stanford.edu)  
**Subject:** RE: PCV13 CE technical report and slides

Dear Almea,

Attached please find the response to all comments from the CDC economic review, an updated slide deck and the technical report.

We are also now preparing the slides for the February 11 presentation.

Best,

Raul

---

**From:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) [<mailto:xdf2@cdc.gov>]  
**Sent:** Tuesday, January 22, 2019 11:53 AM  
**To:** Isturiz, Raul  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD); Mahon, Barbara (CDC/DDID/NCIRD/DBD); Jodar, Luis; Craig, Allen (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD); [gmllee@stanford.edu](mailto:gmllee@stanford.edu)  
**Subject:** [EXTERNAL] RE: PCV13 CE technical report and slides

Dear Raul,  
Attached are comments from the CDC economic review. Please provide your responses to the comments and an updated slide deck to me by February 1<sup>st</sup>. Again as we discussed this short turnaround is so that you can present to the pneumococcal work group on February 11<sup>th</sup> at 11a ET. Please let me know if you have any questions or concerns.  
Thank you,  
Almea

Almea Matanock, MD MS  
NCIRD/DBD/Respiratory Diseases Branch  
Centers for Disease Control and Prevention  
Email: [amatanock@cdc.gov](mailto:amatanock@cdc.gov)  
Phone: 404 718 4364

---

**From:** Isturiz, Raul <(b)(6)>  
**Sent:** Wednesday, December 19, 2018 3:22 PM  
**To:** Matanock, Almea M. (CDC/DDID/NCIRD/DBD) <[xdf2@cdc.gov](mailto:xdf2@cdc.gov)>; [gmllee@stanford.edu](mailto:gmllee@stanford.edu)  
**Cc:** Pilishvili, Tamara (CDC/DDID/NCIRD/DBD) <[tdp4@cdc.gov](mailto:tdp4@cdc.gov)>; Mahon, Barbara (CDC/DDID/NCIRD/DBD) <[bdm3@cdc.gov](mailto:bdm3@cdc.gov)>; Jodar, Luis <(b)(6)>  
**Subject:** PCV13 CE technical report and slides

Dear Drs. Matanock and Lee,

Attached please find the CE technical report and slide deck.

Please let me know if there are any further steps that are required or if I can help in any way.

I take advantage of this opportunity to wish you and your loved ones very happy holidays.

Best,

Raul

Raul E. Isturiz MD FACP  
VP and Regional Head, North America  
Pfizer Vaccines Medical  
Pfizer Inc.

(b)(6)

Executive Administrative Assistant  
Beth Allen

(b)(6)

(b)(6)

**From:** Grabenstein, John D.  
**Sent:** Fri, 3 May 2019 14:24:06 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** FW: Merck - CDC senior leader meeting, 10 May 2019, background materials  
**Attachments:** Merck Rsch Labs Vax ID Meds 2019 May CDC OOD.pdf

**Proprietary**

Best regards, John

**From:** Grabenstein, John D.  
**Sent:** Friday, May 3, 2019 10:22  
**To:** olx1@cdc.gov; Barr, Eliav (b)(6); acs1@cdc.gov; Pope, Kristin (CDC/OID/NCIRD) <kfp7@cdc.gov>; rfk1@cdc.gov; jhm7@cdc.gov; CDCExecSec (CDC) <CDCExecSec@cdc.gov>; Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>  
**Cc:** Villar, Carmen Sachiko (b)(6); Hanna, George (b)(6)  
Annunziato, Paula W. (b)(6)  
**Subject:** Merck - CDC senior leader meeting, 10 May 2019, background materials

**Proprietary**

Dr. Redfield, RADM (Ret) Schuchat, and team:

On behalf of Eliav Barr and the Merck Research Laboratories team, attached please find a read-ahead packet to set the stage for scientific exchange at CDC headquarters on May 10.

The content describes considerable detail about Merck's multiple efforts in preventing and treating infectious diseases of global public-health importance.

Notably, you will find key elements of selected in-line and pipeline products.

We have summarized some of our current interactions with CDC and tee up two topics we propose for on-site discussion:

- Vaccines Program – Reflections on Implementation Challenges
- The President's Plan to Eliminate HIV Transmission in the US by 2030

Please do share these materials with your senior leaders who will be involved with our discussions. Given that the content is proprietary to Merck, please do not distribute it beyond CDC staff with public-health responsibilities along these lines.

Please let me know if any questions arise. We look forward to our visit.

Sincerely, John and the MRL team

John D. Grabenstein, RPh, PhD  
Executive Director, Global Vaccines Medical Affairs

Merck Research Laboratories  
351 N. Sumneytown Pike, UG-2B09  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk (b)(6) cell (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

**From:** Villar, Carmen Sachiko  
**Sent:** Tue, 7 May 2019 19:43:40 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** Pope, Kristin (CDC/DDID/NCIRD/OD); Miles, Carla (CDC/DDPHSIS/CPR) (CTR)  
**Subject:** RE: May 10?  
**Attachments:** Merck Agenda 05.10.2019.v3.docx

Wonderful on multiple fronts. Adding the agenda here from what we got today from the OD. I think they may be adding your name back in. Thanks!!

**Carmen Villar**  
VP, Social Business Innovation, K1-3120  
T: [REDACTED] (b)(6)



---

**From:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Sent:** Tuesday, May 7, 2019 12:50 PM  
**To:** Villar, Carmen Sachiko <[REDACTED] (b)(6)>  
**Cc:** Pope, Kristin (CDC/DDID/NCIRD/OD) <kfp7@cdc.gov>; Miles, Carla (CDC/DDPHSIS/CPR) (CTR) <yiv8@cdc.gov>  
**Subject:** RE: May 10?

**EXTERNAL EMAIL** – Use caution with any links or file attachments.

I did not realize that Dr. Redfield cancelled and I'm sorry to hear that. I did plan to attend but somehow it is no longer on my calendar. I'm looping in Kristin to try to make sure I'm attending the correct sections. And I do plan to return to NCIRD after this detail ends.

Thanks.

Nancy

---

**From:** Villar, Carmen Sachiko <[REDACTED] (b)(6)>  
**Sent:** Monday, May 6, 2019 7:39 AM  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>  
**Subject:** May 10?

Hi Nancy,

I hope all is going well in your new acting role. There will be a team from Merck at CDC on Friday. Dr Redfield was supposed to be there but just cancelled. The team is still coming and meeting with NCHHSTP, NCEZID and NCIRD. Kristin will be there and everyone is looking forward to it. I know it may be sensitive, but there has been a request that you join the meeting if possible. Folks here appreciate your leadership and are assuming you will return to your NCIRD role soon. So, if you are able, we will be there from about 1130-230 and would love to see you. I can share more details if you'd like them. Looking forward to possibly seeing you.

Best,

Carmen

**Carmen Villar**

Vice President, Social Business Innovation

**Merck**

2000 Galloping Hill Road  
Kenilworth, NJ 07033 USA

Email: (b)(6)

T (b)(6)

[merck.com](http://merck.com)



Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.



# Agenda

Friday, May 10, 2019



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

## The Centers for Disease Control and Prevention Welcomes Merck Leadership

*Michael Nally, Executive Vice President, Chief Marketing Officer*

*Paula Annunziato, Vice President, Clinical Research*

*Eliav Barr, Senior Vice President, Medical Affairs*

*Arpa Garay, Senior Vice President, Global Marketing*

*John Grabenstein, Executive Director, Medical Affairs*

*George Hanna, Vice President, Clinical Research*

*Richard Haupt, Vice President, Global Medical Affairs – Vaccines & Infectious Diseases*

*Nicholas Kartsonis, Senior Vice President, Clinical Research*

*Craig Roberts, Associate Vice President, Outcomes Research*

*Paul Schaper, Executive Director, Policy/Govern. Relations*

*David Strutton, Outcomes Research*

*Fabrizio Tondolo, AVP, Medical Affairs*

*Carmen Villar, Vice President, Social Business Innovation*

## Friday, May 10, 2019

CDC Roybal Campus – 1600 Clifton Road, NE, Atlanta, GA 30329

|                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>10:30 – 11:00 a.m.</b></p>  | <p><b>Arrival to CDC</b><br/> <b>Security Check-in &amp; Meet/Greet in lobby of Bldg. 45 (Visitor's Center)</b></p> <ul style="list-style-type: none"> <li>– Teresa Williams, Advance Team &amp; Protocol Specialist, CDC</li> <li>– Brad Bartee, Advance Team &amp; Protocol Specialist, CDC</li> <li>– Mark Byers, Advance Team &amp; Protocol Specialist, CDC</li> </ul> <p>Location: Bldg. 45, Visitors Center</p>                                                                                                                                                                                                                                                                             |
| <p><b>10:45 – 11:15 am</b></p>    | <p><b>Walk to Conference Room 12105, Building 21</b></p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <p><b>11:30 am – 12:00 pm</b></p> | <p><b>Welcome &amp; Leadership to Discuss Collaboration Overall</b><br/> Topic: Merck's Update on Research Pipelines to broadly include: HIV, Ebola, HPV, Maternal and Child Health.<br/> Participants:</p> <ul style="list-style-type: none"> <li>– Robert (Kyle) McGowan, Chief of Staff, CDC</li> <li>– CAPT. Christopher Braden, Deputy Director, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID)</li> <li>– Jonathan Mermin, Director, MD, MPH (RADM, USPHS), National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)</li> <li>– Kristin Pope, Director (Acting), National Center for Immunization and Respiratory Diseases (NCIRD)</li> </ul> |



|                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                  | <ul style="list-style-type: none"> <li>– Amanda Cohn, Chief Medical Officer (Acting), National Center for Immunization and Respiratory Diseases (NCIRD)</li> </ul> <p>Location: Building 21, 12<sup>th</sup> Floor, Room 12105</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 12:00 – 12:45 pm | <p><b>National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) and Center for Global Health (CGH) Leadership</b></p> <p>Topic: More focused discussion on Ebola vaccine and global efforts.</p> <p>Participants:</p> <ul style="list-style-type: none"> <li>– Chris Braden, Deputy Director, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID)</li> <li>– Eric Mast, Deputy Director for Science and Program, Global Immunization Division Center for Global Health (CGH)</li> <li>– Ray Arthur, Co-Lead, CDC Ebola Coordination Team &amp; Lead, Global Disease Detection Operation Center, Emergency Response and Recovery Branch (DGHP) Center for Global Health, (CGH)</li> <li>– Amanda Cohn, Chief Medical Officer (Acting), National Center for Immunization and Respiratory Diseases (NCIRD)</li> </ul> <p>Location: Building 21, 12<sup>th</sup> Floor, Room 12105</p> |
| 12:45 – 1:00 pm  | <b>Break</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 1:00 – 1:45 pm   | <p><b>National Center Immunization and Respiratory Diseases (NCIRD) Leadership</b></p> <p>Topic: Focus on RSV, CMV, HPV, ACIP Issues.</p> <p>Participants:</p> <ul style="list-style-type: none"> <li>– Kristin Pope, Director (Acting), National Center for Immunization and Respiratory Diseases (NCIRD)</li> <li>– Sam Posner, Deputy Director (Acting), NCIRD</li> <li>– Amanda Cohn, Chief Medical Officer (Acting), NCIRD</li> <li>– Mark Pallansch, Director, Division of Viral, NCIRD</li> </ul> <p>Location: Building 21, 12<sup>th</sup> Floor, Room 12105</p>                                                                                                                                                                                                                                                                                                                                           |
| 1:45 – 2:30 pm   | <p><b>National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP) Leadership</b></p> <p>Topic: Focused discussion on HIV efforts.</p> <p>Participants:</p> <ul style="list-style-type: none"> <li>– Jonathan Mermin, MD, MPH (RADM, USPHS), Director, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)</li> <li>– Michelle Owens, Associate Director for Laboratory Science, NCHHSTP</li> <li>– Brian Edlin, Chief Medical Officer, NCHHSTP</li> <li>– John Brooks, Senior Medical Advisor, Division of HIV/AIDS Prevention (DHAP), NCHHSTP</li> <li>– Walid Heneine, Laboratory Branch Chief, Division of HIV/AIDS Prevention (DHAP), NCHHSTP</li> <li>– Gail Bolan, Director, Division of Sexually Transmitted Disease Prevention (DSTDP), NCHHSTP</li> <li>– Raul Romaguera, Deputy Director DSTDP, NCHHSTP</li> </ul>                                       |

|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                       | <ul style="list-style-type: none"> <li>– <i>Laura Bachman, Medical Officer, DSTDP, NCHHSTP</i></li> <li>– <i>Kyle Bernstein, Chief Epidemiology and Surveillance, DSTDP, NCHHSTP</i></li> <li>– <i>Bob Kirkcaldy, Medical Officer, DSTDP, NCHHSTP</i></li> <li>– <i>Blythe Ryerson, Associate Director for Science, Division of Viral Hepatitis (DVH), NCHHSTP</i></li> <li>– <i>Amanda Campbell, Deputy to the Chief of Staff, CDC</i></li> </ul> <p><i>Location: Building 21, 12<sup>th</sup> Floor, Room 12105</i></p> |
| <b>2:30-2:45 pm</b>   | <p><b>Departure from CDC</b></p> <p>Escorted to Visitor's Center entrance</p>                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>2:45 - 3:15 pm</b> | <p><b><i>Transit to Airport</i></b></p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

**From:** Grabenstein, John D.  
**Sent:** Tue, 12 Nov 2019 00:26:08 +0000  
**To:** Choi, Mary Joung (CDC/DDID/NCEZID/DHCPP); Messonnier, Nancy (CDC/DDID/NCIRD/OD); Cohn, Amanda (CDC/DDID/NCIRD/OD)  
**Cc:** Collier, Beth-Ann Griswold; Macareo, Louis Robert; Wolf, Jayanthi; Shah, Anant C; Soloski, Drew  
**Subject:** European registration of Merck V920 Ebola vaccine  
**Attachments:** ema-combined-h-4554-en.docx

Dr. Messonnier, CAPT Cohn, Dr. Choi,

This is a courtesy message to alert you that the European Medicines Agency (EMA) today granted registration to Merck's Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live), also known as V920 and now 'Ervebo.' EMA reviewed this vaccine under EMA's [accelerated assessment](#) program and it was granted conditional marketing authorization within the EU.

Please allow me to emphasize that this European decision has no bearing on the US status or availability of V920, insofar as the US Food & Drug Administration (FDA) has not yet reached a decision about V920. V920 remains an Investigational New Drug (IND) within the USA.

This EMA website reports the product in its CHMP-recommended status of mid-October 2019. The site will change shortly, we expect.

<https://www.ema.europa.eu/en/medicines/human/summaries-opinion/ervebo>.

I have attached the European Summary of Product Characteristics (SmPC), for your background information. This document or a similar version will appear at the EMA website in coming days. We would expect any language that FDA might approve sometime in the future to be different, to some greater or lesser extent that we cannot currently anticipate. We make no promise about what future action, if any, FDA may take.

Best regards, John

John D. Grabenstein, RPh, PhD  
Executive Director, Global Medical Affairs -- Vaccines  
Merck Research Laboratories  
351 N. Sumneytown Pike, UG-2B09  
North Wales, PA 19454-2505

[www.MerckVaccines.com](http://www.MerckVaccines.com)

desk (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at

<http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## **1. NAME OF THE MEDICINAL PRODUCT**

Ervebo solution for injection  
Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

One dose (1 mL) contains:

Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP<sup>1,2</sup> live, attenuated) ≥72 million pfu<sup>3</sup>

<sup>1</sup>Recombinant Vesicular Stomatitis Virus (rVSV) strain Indiana with a deletion of the VSV envelope glycoprotein (G) replaced with the Zaire Ebola Virus (ZEBOV) Kikwit 1995 strain surface glycoprotein (GP)

<sup>2</sup>Produced in Vero cells.

<sup>3</sup>pfu= plaque-forming units

This product contains genetically modified organisms (GMOs).  
This vaccine contains a trace amount of rice protein. See section 4.3.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Solution for injection  
The solution is a colourless to slightly brownish-yellow liquid.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Ervebo is indicated for active immunization of individuals 18 years of age or older to protect against Ebola Virus Disease (EVD) caused by Zaire Ebola virus (see sections 4.2, 4.4 and 5.1).

The use of Ervebo should be in accordance with official recommendations.

### **4.2 Posology and method of administration**

Ervebo should be administered by a trained healthcare worker.

#### Posology

Individuals 18 years of age or older: one dose (1 mL) (see section 5.1).

The need for a booster dose has not been established.

#### *Paediatric population*

The safety, immunogenicity and efficacy of Ervebo in children aged 1 to 17 years have not yet been established (see sections 4.8 and 5.1).



### Method of administration

For precautions to be taken before administering the vaccine, see section 4.4.

For precautions regarding thawing, handling and disposal of the vaccine, see section 6.6.

Ervebo should be administered by the intramuscular (IM) route. The preferred site is the deltoid area of the non-dominant arm or in the higher anterolateral area of the thigh. Do not inject the vaccine intravascularly. No data are available for administration via the subcutaneous or intradermal routes.

Cover the vaccination injection site or any vesicles with an adequate bandage (e.g. any adhesive bandage or gauze and tape) that provides a physical barrier to protect against direct contact (see sections 4.4 and 5.3). The bandage may be removed when there is no visible fluid leakage.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

### **4.3 Contraindications**

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 or to rice protein listed in section 2.

### **4.4 Special warnings and precautions for use**

#### Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

#### Hypersensitivity

Close monitoring is recommended following vaccination for the early signs of anaphylaxis or anaphylactoid reactions. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

#### Duration of protection

Vaccination with Ervebo may not result in protection in all vaccinees. Vaccine efficacy has been established in the period  $\geq 10$  to  $\leq 31$  days after vaccination, however the duration of protection is not known (see section 5.1). **The use of other Ebola control measures should therefore not be interrupted.**

Vaccination of contacts of Ebola cases should occur as soon as possible (see section 5.1).

#### Standard precautions when caring for patients with known or suspected Ebola disease

Vaccination with Ervebo does not eliminate the necessity of standard precautions when caring for patients with known or suspected Ebola disease. **All healthcare workers and other ancillary providers who have been vaccinated should not alter their practices with regard to safe injection, hygiene, and personal protective equipment (PPE) after vaccination.**

Healthcare workers caring for patients with suspected or confirmed Ebola virus should apply extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding. Samples taken from humans and



animals for investigation of Ebola infection should be handled by trained staff and processed in suitably equipped laboratories.

Vaccine administrators should counsel vaccinees to continue to protect themselves with adequate measures.

#### Immunocompromised individuals

Safety and efficacy of Ervebo have not been assessed in immunocompromised individuals. Immunocompromised individuals may not respond as well as immunocompetent individuals to Ervebo. As a precautionary measure, it is preferable to avoid the use of Ervebo in individuals with known immunocompromised conditions or receiving immunosuppressive therapy, including the following conditions:

- Severe humoral or cellular (primary or acquired) immunodeficiency, e.g. severe combined immunodeficiency, agammaglobulinemia, and AIDS or symptomatic HIV infection. A CD4+ T-lymphocyte count threshold for use in asymptomatic HIV-positive individuals has not been established.
- Current immunosuppressive therapy, including high doses of corticosteroid. This does not include individuals who are receiving topical, inhaled or low-dose parenteral corticosteroids (e.g. for asthma prophylaxis or replacement therapy).
- Diseases of the blood such as leukaemia, lymphomas of any type, or other malignant neoplasms affecting the haematopoietic and lymphatic systems.
- Family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.

#### Pregnant and breast-feeding women

As a precautionary measure, it is preferable to avoid the use of Ervebo during pregnancy. See section 4.6.

#### Transmission

Vaccine virus might be present in biological fluids such as blood, urine, saliva, semen, vaginal fluids, aqueous humor, breast milk, faeces, sweat, amniotic fluid, and placenta. Vaccine virus RNA has been detected by PCR in the plasma of most of the adult subjects. Vaccine virus RNA was mainly detected from Day 1 to Day 7. Shedding of vaccine virus has been detected by PCR in urine or saliva in 19 out of 299 adult subjects and in skin vesicles in 4 out of 10 adult subjects. The vaccine virus RNA was detected in a skin vesicle at 12 days post-vaccination in one of the four subjects.

Viral shedding was observed more frequently in children and adolescents (28/39) compared to adults.

Transmission of vaccine virus through close personal contact is accepted as a theoretical possibility. Vaccine recipients should avoid close contact with and exposure of high-risk individuals to blood and bodily fluids for at least 6 weeks following vaccination. High-risk individuals include:

- Immunocompromised individuals and individuals receiving immunosuppressive therapy (see section above),
- Pregnant or breast-feeding women (see section 4.6),
- Children <1 year of age.

Individuals who develop vesicular rash after receiving the vaccine should cover the vesicles until they heal to minimize the risk of possible transmission of vaccine virus through open vesicles. Dispose of contaminated bandages following institutional guidelines or WHO healthcare waste management policy. See section 5.3.

Inadvertent transmission of vaccine virus to animals and livestock is also theoretically possible, see below.

Individuals administered Ervebo should not donate blood for at least 6 weeks post-vaccination.

#### Transmission to animals and livestock

Transmission of vaccine virus through close contact with livestock is accepted as a theoretical possibility. Vaccine recipients should attempt to avoid exposure of livestock to blood and bodily fluids for at least 6 weeks following vaccination. Individuals who develop vesicular rash after receiving the vaccine should cover the vesicles until they heal. Dispose of contaminated bandages following institutional guidelines or WHO healthcare waste management policy. See section 5.3.

#### Concurrent illness

Vaccination should be postponed in subjects experiencing moderate or severe febrile illness. The presence of a minor infection should not result in deferral of vaccination.

#### Thrombocytopenia and coagulation disorders

The vaccine should be given with caution to individuals with thrombocytopaenia or any coagulation disorder because bleeding or bruising may occur following an intramuscular administration in these individuals.

#### Protection against filovirus disease

The vaccine will not prevent disease caused by Filoviruses other than Zaire Ebola virus.

#### Impact to serological testing

Following vaccination with Ervebo, individuals may test positive for Ebola glycoprotein (GP) nucleic acids, antigens, or antibodies against Ebola GP, which are targets for certain Ebola diagnostic tests. Therefore, diagnostic testing for Ebola should target non-GP sections of the Ebola virus.

#### Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, and is considered to be essentially sodium-free.

### **4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed.

As there are no data on co-administration of Ervebo with other vaccines, the concomitant use of Ervebo with other vaccines is not recommended.

Immune globulin (IG), blood or plasma transfusions should not be given concomitantly with Ervebo. Administration of immune globulins, blood or plasma transfusions administered 3 months before or up to 1 month after Ervebo administration may interfere with the expected immune response.

It is unknown whether concurrent administration of antiviral medication including interferons could impact vaccine virus replication and efficacy.

### **4.6 Fertility, pregnancy and lactation**

#### Pregnancy

There are limited amount of data (less than 300 pregnancy outcomes) from the use of Ervebo in pregnant women, or women who became pregnant after receiving the vaccine. The safety of Ervebo has not been established in pregnant women.

As there are limitations to available data, including the small number of cases, caution should be exercised in drawing conclusions. Lack of reliable data on background rates of pregnancy and neonatal outcomes in the affected regions also makes a contextual assessment of the data challenging.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of Ervebo during pregnancy. Nevertheless considering the severity of EVD, vaccination should not be withheld when there is a clear risk of exposure to Ebola infection.

Pregnancy should be avoided for 2 months following vaccination. Women of child-bearing potential should use an effective contraceptive method.

#### Breast-feeding

It is unknown whether the vaccine virus is secreted in human milk.

A risk to the newborns/infants from breast-feeding by vaccinated mothers cannot be excluded.

Evaluation of the vaccine virus in animal milk has not been conducted. When Ervebo is administered to female rats, antibodies against the vaccine virus were detected in offspring, likely due to acquisition of maternal antibodies via placental transfer during gestation and via lactation. See section 5.3.

A decision must be made whether to discontinue breast-feeding or to abstain from Ervebo taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. In certain circumstances, where alternatives to breastfeeding are limited, the immediate need and health benefits to the infant should be taken into consideration and balanced with the mother's need for Ervebo. Both may present compelling needs that should be considered before vaccination of the mother.

#### Fertility

There are no data on fertility effects in humans.

Animal studies in female rats do not indicate harmful effects (see section 5.3).

### **4.7 Effects on ability to drive and use machines**

No studies on the effects of Ervebo on the ability to drive and use machines have been performed.

Ervebo has no or negligible influence on the ability to drive and use machines.

### **4.8 Undesirable effects**

#### Summary of the safety profile

Anaphylaxis was reported very rarely (0.006%) in clinical trials.

The most common injection-site adverse reactions were injection-site pain (70.3%), swelling (16.7%) and erythema (13.7%).

The most common systemic adverse reactions reported following vaccination with Ervebo were headache (36.9%), pyrexia (34.3%), myalgia (32.5%), fatigue (18.5%), arthralgia (17.1%), nausea

(8.0%), chills (6.3%), arthritis (3.7%), rash (3.6%), hyperhidrosis (3.2%), and abdominal pain (1.4%). In general, these reactions were reported within 7 days after vaccination, were mild to moderate in intensity, and had short duration (less than 1 week).

#### Tabulated list of adverse reactions

Frequencies are reported as:

Very common ( $\geq 1/10$ ), Common ( $\geq 1/100$  to  $< 1/10$ ), Uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), Rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), Very rare ( $< 1/10,000$ ), Not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Table 1: Tabulated summary of adverse reactions considered related to vaccination

| MedDRA-System Organ Class                             | Adverse Reactions                                                                               | Frequency   |
|-------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------------|
| Immune system disorders:                              | Anaphylactic reaction                                                                           | Very Rare   |
| Nervous system disorders:                             | Headache                                                                                        | Very common |
| Gastrointestinal disorders:                           | Abdominal pain<br>Nausea                                                                        | Common      |
| Skin and subcutaneous tissue disorders:               | Rash <sup>§</sup>                                                                               | Common      |
| Musculoskeletal and connective tissue disorders:      | Arthralgia <sup>§</sup>                                                                         | Very common |
|                                                       | Myalgia                                                                                         |             |
|                                                       | Arthritis <sup>§</sup>                                                                          | Common      |
| General disorders and administration site conditions: | Pyrexia<br>Fatigue<br>Injection site pain<br>Injection site erythema<br>Injection site swelling | Very common |
|                                                       | Chills<br>Hyperhidrosis (sweats)                                                                | Common      |

<sup>§</sup>See description of selected adverse reactions.

#### Description of selected adverse reactions

##### *Arthralgia and arthritis*

Arthralgia was generally reported in the first few days following vaccination, was mild to moderate in intensity, and resolved within one week after onset. Arthritis (arthritis, joint effusion, joint swelling, osteoarthritis, monoarthritis or polyarthritis) was generally reported within the first few weeks following vaccination. In clinical trials with reports of arthritis, the median onsets were between 10 and 12 days (range from 0 to 25 days). Arthritis has been reported by subjects in clinical trials at a frequency that ranged from 0% in several protocols to 23.5% in one Phase 1 study. The majority of arthritis reactions were mild to moderate in severity. The median duration of arthritis across clinical trials in which arthritis was reported ranged from 2 days to 81.5 days (including duration of recurrent arthritis) with a maximum of 330 days. The reasons for differences in arthritis reporting across trials are not known but may be due to differences in study populations or outcome reporting. In the Phase 1 study with the highest rate of arthritis, 6 of 24 patients (25%) who reported arthritis after vaccination had persistent joint symptoms two years after vaccination. In a small number of subjects, the vaccine virus was recovered from joint effusion samples, suggestive of a virally-mediated process post-vaccination.

##### *Rash*

Rash was characterized in a variety of ways including generalized rash (2.3%), vesicular rash (0.5%), dermatitis (0.3%), or cutaneous vasculitis (0.01%) in clinical trials. In different trials, rash was reported with median onsets of 7.5 to 10.5 days (range from 0 to 47 days). The median durations



reported were between 6 to 18 days. In 6 out of 18 subjects tested, the vaccine virus was detected in rashes (described as dermatitis, vesicles or cutaneous vasculitis lesions) suggesting a virally mediated process post-vaccination.

#### *Transient decrease in white blood cells*

Transient decreases in counts of lymphocytes, neutrophils and total white blood cells in the first 3 days following vaccination have been observed very commonly in Phase 1/2 studies; these events generally resolved after the first week post-vaccination. No adverse events of infections were observed in Phase 1/2 trials.

#### Paediatric population

Across the Phase 1 through Phase 3 trials, 234 children and adolescents 6 to 17 years of age received a dose of Ervebo.

The safety profile of Ervebo in children and adolescents 6 to 17 years of age was generally similar to that observed in adults.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

### **4.9 Overdose**

No cases of overdose have been reported.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Vaccines, Viral Vaccine, ATC code: J07BX02

#### Mechanism of action

Ervebo consists of a live, attenuated recombinant vesicular stomatitis virus-based vector expressing the envelope glycoprotein gene of Zaire Ebola virus (rVSVΔG-ZEBOV-GP). Immunization of subjects with the vaccine results in an immune response and protection from Zaire Ebola Virus Disease (EVD). The relative contributions of innate, humoral and cell-mediated immunity to protection from Zaire Ebola virus are unknown.

#### Clinical efficacy

The clinical development program included four Phase 2/3 (Protocols 009-012) clinical trials. All subjects received a single dose of vaccine. Clinical efficacy of Ervebo was assessed in Protocol 010.

Protocol 010 (Ring vaccination study) was a Phase 3 open-label cluster-randomized trial of ring vaccination (vaccinating contacts and contacts of contacts [CCCs] of index Ebola cases) which evaluated efficacy and safety of Ervebo in Guinea. In this trial, 9,096 subjects ≥18 years of age who were considered CCCs of an index case with laboratory-confirmed EVD were randomized to immediate (4,539 subjects in 51 clusters) or 21 days delayed (4,557 subjects in 47 clusters) vaccination with Ervebo. Of those 9,096 subjects, 4,160 received Ervebo (2,119 subjects were vaccinated in the immediate arm and 2,041 subjects were vaccinated in the delayed arm). The median age of consenting CCCs was 35 years old. The final primary analysis included 2,108 subjects (51

clusters) vaccinated in the immediate arm and 1,429 subjects (46 clusters) eligible and consented on Day 0 in the delayed arm.

The final primary analysis was to assess efficacy against laboratory confirmed EVD by comparing incidence of cases occurring 10 to 31 days post-randomization for those vaccinated in the immediate vaccination rings versus incidence of cases for subjects who consented on Day 0 in the delayed vaccination rings. Vaccine efficacy was 100% (unadjusted 95% CI: 63.5% to 100%; 95% CI adjusted for multiplicity: 14.4% to 100%) (0 cases in the immediate arm; 10 cases in 4 rings in the delayed arm). Randomization was stopped after an interim analysis with a  $p=0.0036$  that did not meet the pre-specified alpha level of 0.0027. Of the 10 cases, 7 were in contacts, and 3 in contacts-of-contacts. Uncertainties remain as to the level, duration and type of protection given the methodological limitations and the exceptional circumstances experienced during the trial.

### Clinical immunogenicity

No immune correlates of protection have been defined to date.

Protocol 009 Partnership for Research on Ebola Vaccines in Liberia (PREVAIL) was a Phase 2 randomized, double-blind, placebo-controlled trial which evaluated the safety and immunogenicity of Ebola vaccine candidates including Ervebo. This trial compared Ervebo to normal saline placebo in 1,000 adults  $\geq 18$  years of age in Liberia.

Protocol 011 named Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE) was a Phase 2/3 randomized open-label trial which evaluated safety and immunogenicity of Ervebo in adults  $\geq 18$  years of age working in healthcare facilities or on frontline activities related to the Ebola response in Sierra Leone. In this trial, 8,673 adult subjects were enrolled and 8,651 with valid consents randomized to immediate (within 7 days of enrolment) or deferred (18 to 24 weeks after enrolment) vaccination with Ervebo. An immunogenicity sub-study included 508 subjects who were vaccinated and provided samples for the assessment of immunogenicity.

Protocol 012 was a Phase 3 randomized, double-blind, placebo-controlled trial which evaluated the safety and immunogenicity of three consistency lots and a high dose lot (approximately five times higher than the dose in consistency lots and dose used in other Phase 2/3 trials) of Ervebo compared to normal saline placebo. A total of 1,197 healthy subjects 18 to 65 years of age were enrolled in the US, Canada, and Spain.

Immunogenicity testing has been performed in Protocol 009, Protocol 011 and Protocol 012, and includes the assessment of binding immunoglobulin G (IgG) specific to purified Kikwit ZEBOV GP by validated enzyme linked immunosorbent assay (GP-ELISA) as well as validated neutralization of vaccine virus by a plaque reduction neutralization test (PRNT).

As shown in Tables 2 and 3, the geometric mean titers (GMT) of GP-ELISA and PRNT increased from pre-vaccination to post-vaccination. Over 93.8% of vaccine recipients met seroresponse criteria defined as a  $\geq 2$ -fold increase from baseline and  $\geq 200$  EU/mL at any time post-vaccination by GP-ELISA and over 80.4% of subjects met seroresponse criteria defined as a  $\geq 4$ -fold increase from baseline at any time post-vaccination by PRNT. Over 80.1% of subjects continued to meet the seroresponse criteria for GP-ELISA and over 63.5% of vaccine recipients continued to meet seroresponse criteria for PRNT at 12 months. The clinical relevance of the immunogenicity data is currently not known.

Efficacy data was obtained in Protocol 010 in Guinea and immunogenicity data was obtained in Protocol 009 in Liberia, Protocol 011 in Sierra Leone, and Protocol 012 in the United States, Canada, and Europe. Baseline seropositivity, gamma irradiation of specimens to reduce risk of wild-type Ebola virus infection of laboratory workers, and other factors may impact the immune response to vaccine, which results in a higher immune response in Protocol 012. Although the clinical relevance of the GP-ELISA GMT as well as seroresponse is currently not known, based on available data it is expected that

vaccine efficacy would apply to subjects from Guinea, Liberia, Sierra Leone, the United States, Canada, Europe, or other parts of the world.

Table 2. Summary of Geometric Mean Titers for the GP-ELISA from Protocols 009, 011 and 012 Clinical Trials

| <b>Trial</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <b>Baseline<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 1<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 6<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 12*<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 24<br/>GMT (n)<br/>[95% CI]</b> |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|-----------------------------------------|-----------------------------------------|-------------------------------------------|------------------------------------------|
| <b>Protocol 009§</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 117.9 (464)<br>[107.9, 128.7]            | 994.7 (475)<br>[915.0, 1,081.3]         | 712.2 (477)<br>[659.4, 769.3]           | 661.4 (475)<br>[613.2, 713.4]             | NA                                       |
| <b>Protocol 011§</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 92.7 (503)<br>[85.3, 100.9]              | 964.3 (443)<br>[878.7, 1,058.3]         | 751.8 (383)<br>[690.6, 818.4]           | 760.8 (396)<br>[697.6, 829.8]             | NA                                       |
| <b>Protocol 012</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                          |                                         |                                         |                                           |                                          |
| Combined<br>Consistency Lots<br>Group                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | < 36.11 (696)<br>[<36.11, <36.11]        | 1,262.0 (696)<br>[1,168.9, 1,362.6]     | 1,113.4 (664)<br>[1,029.5, 1,204.0]     | 1,078.4 (327)<br>[960.6, 1,210.7]         | 920.3 (303)<br>[820.4, 1,032.3]          |
| High Dose Group                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | < 36.11 (219)<br>[<36.11, <36.11]        | 1,291.9 (219)<br>[1,126.9, 1,481.2]     | 1,189.5 (215)<br>[1,036.7, 1,364.9]     | 1,135.5 (116)<br>[934.8, 1,379.3]         | 1,009.1 (105)<br>[830.0, 1,226.7]        |
| Placebo Group                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | < 36.11 (124)<br>[<36.11, <36.11]        | < 36.11 (124)<br>[<36.11, <36.11]       | < 36.11 (123)<br>[<36.11, <36.11]       | < 36.11 (65)<br>[<36.11, <36.11]          | < 36.11 (65)<br>[<36.11, <36.11]         |
| <p>The Full Analysis Set population was the primary population for the immunogenicity analyses in Protocols 009 and 011 and consists of all vaccinated subjects with serology data and had a serum sample collected within an acceptable day range.</p> <p>The Per-Protocol Immunogenicity Population was the primary population for the immunogenicity analyses in Protocol 012 and includes all subjects who were compliant with the protocol, received vaccination, were seronegative at Day 1, and had a serum sample at one or more timepoints collected within an acceptable day range.</p> <p>n = Number of subjects contributing to the analysis.</p> <p>CI = Confidence interval; GP-ELISA = Anti-Glycoprotein Human Enzyme-Linked Immunosorbent Assay (EU/mL); GMT = Geometric mean titer</p> <p>*Protocol 011 from Month 9-12.</p> <p>§Protocols 009 and 011 used gamma irradiation of specimens to reduce risk of wild-type Ebola virus infection of laboratory workers</p> |                                          |                                         |                                         |                                           |                                          |

Table 3. Summary of Geometric Mean Titers for the PRNT from Protocols 009, 011 and 012 Clinical Trials

| <b>Trial</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <b>Baseline<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 1<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 6<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 12*<br/>GMT (n)<br/>[95% CI]</b> | <b>Month 24<br/>GMT (n)<br/>[95% CI]</b> |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|-----------------------------------------|-----------------------------------------|-------------------------------------------|------------------------------------------|
| <b>Protocol 009§</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | < 35 (428)<br>[<35, <35]                 | 116.8 (477)<br>[106.0, 128.8]           | 76.8 (477)<br>[69.9, 84.4]              | 100.4 (476)<br>[91.4, 110.3]              | NA                                       |
| <b>Protocol 011§</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | < 35 (438)<br>[<35, <35]                 | 116.0 (437)<br>[105.7, 127.4]           | 95.3 (382)<br>[86.3, 105.3]             | 119.9 (396)<br>[107.9, 133.2]             | NA                                       |
| <b>Protocol 012</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                          |                                         |                                         |                                           |                                          |
| Combined<br>Consistency Lots<br>Group                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | < 35 (696)<br>[<35, <35]                 | 202.1 (696)<br>[187.9, 217.4]           | 266.5 (664)<br>[247.4, 287.0]           | 271.4 (327)<br>[243.4, 302.7]             | 267.6 (302)<br>[239.4, 299.2]            |
| High Dose Group                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | < 35 (219)<br>[<35, <35]                 | 236.1 (219)<br>[207.4, 268.8]           | 302.1 (215)<br>[265.2, 344.1]           | 323.7 (116)<br>[269.5, 388.8]             | 342.5 (105)<br>[283.4, 414.0]            |
| Placebo Group                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | < 35 (124)<br>[<35, <35]                 | < 35 (123)<br>[<35, <35]                | < 35 (123)<br>[<35, <35]                | < 35 (65)<br>[<35, <35]                   | < 35 (65)<br>[<35, <35]                  |
| <p>The Full Analysis Set population was the primary population for the immunogenicity analyses in Protocols 009 and 011 and consists of all vaccinated subjects with serology data and had a serum sample collected within an acceptable day range.</p> <p>The Per-Protocol Immunogenicity Population was the primary population for the immunogenicity analyses in Protocol 012 and includes all subjects who were compliant with the protocol, received vaccination, were seronegative at Day 1, and had a serum sample at one or more</p> |                                          |                                         |                                         |                                           |                                          |



timepoints collected within an acceptable day range.

n = Number of subjects contributing to the analysis.

CI = Confidence interval; GMT = Geometric mean titer; PRNT = Plaque Reduction Neutralization Test

\*Protocol 011 from Month 9-12

§Protocols 009 and 011 used gamma irradiation of specimens to reduce risk of wild-type Ebola virus infection of laboratory workers

### Paediatric population

Efficacy in children has not been assessed. In a Phase 1 trial in children 6 to 17 years of age (median age = 10), non-validated ELISA and Pseudovirion Neutralization Assay (PsVNA) results at Day 28 and Day 180 post-vaccination were similar to those observed in adults in the same study (see also sections 4.4 and 4.8).

The European Medicines Agency has deferred the obligation to submit the results of studies with Ervebo in one or more subsets of the paediatric population in prevention of Ebola disease (see section 4.2 for information on paediatric use).

---

This medicinal product has been authorised under a so-called 'conditional approval' scheme.

This means that further evidence on this medicinal product is awaited.

The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

## **5.2 Pharmacokinetic properties**

Not applicable.

## **5.3 Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and toxicity to reproduction and development.

When Ervebo was administered to female rats, antibodies against the vaccine virus were detected in foetuses and offspring, likely due to trans-placental transfer during gestation and with the acquisition of maternal antibodies during lactation, respectively (see section 4.6).

Ervebo administered to female rats had no effects on mating performance, fertility, or embryonic/foetal development.

Ervebo administered to female rats had no effects on development or behaviour of the offspring.

### Environmental Risk Assessment (ERA)

The vaccine virus is a Genetically Modified Organism (GMO). An ERA was conducted to determine the potential impact of this vaccine on human health and the environment. Because this vaccine is based on VSV, a known pathogen in livestock (e.g. horses, cattle, pigs), the risk assessment included species that are relevant for the wild type (wt) VSV backbone of this vaccine.

In a biodistribution study conducted in non-human primates, vaccine virus RNA was detected in lymphoid organs up to 112 days post-vaccination. However, infectious virus was detected at Day 1 and persistent infectious virus was not detected at any subsequent timepoints measured (Days 56, 84 and 112).

Based on limited shedding in adults, the results of a toxicity study in non-human primates, and lack of horizontal transmission in pigs, the overall risk of Ervebo to human health and the environment is



considered negligible. However, as a precaution, vaccinees should attempt to avoid exposure of livestock to blood and bodily fluids for at least 6 weeks following vaccination to avoid the theoretical risk of spread of the vaccine virus. People who develop vesicular rash after receiving the vaccine should cover the vesicles until they heal. Cover the vaccination site or any vesicles with an adequate bandage (e.g. any adhesive bandage or gauze and tape) that provides a physical barrier to protect against direct contact with vesicle fluid (see section 4.2). The bandage may be removed when there is no visible fluid leakage. To avoid unintended exposure to livestock, ensure medical waste and other cleaning materials do not come in contact with livestock.

See sections 4.4 and 6.6 for further information.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Recombinant human serum albumin  
Trometamol buffer  
Water for injections  
Hydrochloric acid (for pH-adjustment)  
Sodium hydroxide (for pH-adjustment)

### **6.2 Incompatibilities**

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

### **6.3 Shelf life**

3 years

### **6.4 Special precautions for storage**

Store and transport frozen at -80°C to -60°C.

After thawing, the vaccine should be used immediately; however, in-use stability data have demonstrated that once thawed, the vaccine can be stored for up to 14 days at 2°C to 8°C prior to use. At the end of 14 days, the vaccine should be used or discarded. Upon removal from the freezer, the product should be marked with both the date that it was taken out of the freezer and also a new discard date (in place of the labelled expiry date). Once thawed, the vaccine cannot be re-frozen.

Keep the vial in the outer carton in order to protect from light.

### **6.5 Nature and contents of container**

Solution for 1 dose in a vial (type I glass) with a stopper (chlorobutyl) and a flip-off plastic cap with aluminium seal.

Pack size of 10 vials.

### **6.6 Special precautions for disposal and other handling**

- The vaccine is stored frozen at -80°C to -60°C and should be removed from the freezer and thawed in less than 4 hours until no visible ice is present. Do not thaw the vial in a refrigerator as it is not guaranteed that the vial will thaw in less than 4 hours. The thawed vial should then be gently inverted several times prior to withdrawal with the syringe. The vaccine should appear

as a colourless to slightly brownish-yellow liquid with no particulates visible. Discard the vaccine if particulates are present.

- Withdraw the entire content of the vaccine from the vial using a sterile needle and syringe.

If feasible, the waste liquid from eye washes should be collected and decontaminated before discarding into the drain.

Any unused vaccine or waste material should be disposed in compliance with the institutional guidelines for genetically modified organisms or biohazardous waste, as appropriate.

If breakage/spillage were to occur, disinfectants such as aldehydes, alcohols and detergents are proven to reduce viral infection potential after only a few minutes.

## **7. MARKETING AUTHORISATION HOLDER**

Merck Sharp & Dohme B.V.  
Waarderweg 39  
2031 BN Haarlem  
The Netherlands

## **8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/19/1392/001

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: {DD month YYYY}

## **10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

## **ANNEX II**

- A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**
- E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION**

**A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer(s) of the biological active substance(s)

Burgwedel Biotech GmbH  
Im Langen Felde 5  
30938 Burgwedel  
Germany

Name and address of the manufacturer(s) responsible for batch release

Burgwedel Biotech GmbH  
Im Langen Felde 5  
30938 Burgwedel  
Germany

In view of the declared Public Health Emergency of International Concern and in order to ensure early supply this medicinal product is subject to a time-limited exemption allowing reliance on batch control testing conducted in the registered site(s) that are located in a third country. This exemption is subject to annual review and in any case ceases to be valid on 31 July 2022. Implementation of EU based batch control arrangements, including the necessary variations to the terms of the marketing authorisation, has to be completed by the 31 July 2022 at the latest, in line with the agreed plan for this transfer of testing. A progress report has to be included in the annual renewal application.

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

#### **E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION**

This being a conditional marketing authorisation and pursuant to Article 14-a(4) of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

| <b>Description</b>                                                                                                                                                                                   | <b>Due date</b> |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| The MAH should provide additional data to confirm that the active substance (AS) process is properly validated. Process and batch data from at least 3 representative AS batches should be provided. | 29 May 2020     |
| The MAH should provide additional data to confirm that the finished product (FP) process is properly validated. Process and batch data from at least 3 representative FP batches should be provided. | 30 Oct 2020     |
| The MAH should provide comprehensive comparability data confirming that the commercial product manufactured at the Burgwedel site is representative of the material used in the clinical trials.     | 29 May 2020     |
| The MAH should complete master cell banks (MCB)/working cell bank (WCB) qualification to include also tests for specified viruses.                                                                   | 30 Oct 2020     |
| The MAH should provide additional qualification data for the critical reagent used in the identity test (quality control release test for AS and FP).                                                | 31 Jan 2020     |
| The MAH should develop and introduce an active substance in-process control for total protein with appropriate acceptance.                                                                           | 29 May 2020     |

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****SOLUTION FOR INJECTION IN VIAL - PACK OF 10****1. NAME OF THE MEDICINAL PRODUCT**

Ervebo solution for injection  
Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

One dose (1 mL):  
Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live attenuated) ≥72 million pfu

**3. LIST OF EXCIPIENTS**

Recombinant human serum albumin, trometamol buffer, water for injections, hydrochloric acid, sodium hydroxide

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection  
10 vials

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Intramuscular use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN****7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store and transport frozen at -80°C to -60°C.  
Do not thaw the vial in a refrigerator. Do not refreeze.  
Keep the vial in the outer carton to protect from light.



|                                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</b> |
|--------------------------------------------------------------------------------------------------------------------------------------------------|

This product contains genetically modified organisms.

Any unused vaccine or waste material should be disposed of in compliance with the institutional guidelines for genetically modified organisms or biohazardous waste, as appropriate.

|                                                                   |
|-------------------------------------------------------------------|
| <b>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</b> |
|-------------------------------------------------------------------|

Merck Sharp & Dohme B.V.  
Waarderweg 39  
2031 BN Haarlem  
The Netherlands

|                                              |
|----------------------------------------------|
| <b>12. MARKETING AUTHORISATION NUMBER(S)</b> |
|----------------------------------------------|

EU/1/19/1392/001 - pack of 10

|                         |
|-------------------------|
| <b>13. BATCH NUMBER</b> |
|-------------------------|

Lot

|                                              |
|----------------------------------------------|
| <b>14. GENERAL CLASSIFICATION FOR SUPPLY</b> |
|----------------------------------------------|

|                                |
|--------------------------------|
| <b>15. INSTRUCTIONS ON USE</b> |
|--------------------------------|

|                                   |
|-----------------------------------|
| <b>16. INFORMATION IN BRAILLE</b> |
|-----------------------------------|

Justification for not including Braille accepted

|                                           |
|-------------------------------------------|
| <b>17. UNIQUE IDENTIFIER – 2D BARCODE</b> |
|-------------------------------------------|

2D barcode carrying the unique identifier included.

|                                                    |
|----------------------------------------------------|
| <b>18. UNIQUE IDENTIFIER - HUMAN READABLE DATA</b> |
|----------------------------------------------------|

PC  
SN  
NN

|                                                                                              |
|----------------------------------------------------------------------------------------------|
| <b>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</b><br><b>VIAL LABEL</b> |
|----------------------------------------------------------------------------------------------|

|                                                                        |
|------------------------------------------------------------------------|
| <b>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</b> |
|------------------------------------------------------------------------|

Ervebo solution for injection  
rVSVΔG-ZEBOV-GP, live  
IM

|                                    |
|------------------------------------|
| <b>2. METHOD OF ADMINISTRATION</b> |
|------------------------------------|

|                       |
|-----------------------|
| <b>3. EXPIRY DATE</b> |
|-----------------------|

EXP

|                                                            |
|------------------------------------------------------------|
| <b>4. BATCH NUMBER&lt;, DONATION AND PRODUCT CODES&gt;</b> |
|------------------------------------------------------------|

Lot

|                                                    |
|----------------------------------------------------|
| <b>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</b> |
|----------------------------------------------------|

1 dose

|                 |
|-----------------|
| <b>6. OTHER</b> |
|-----------------|

This product contains GMO.

## **B. PACKAGE LEAFLET**

## **Package leaflet: Information for the user**

### **Ervebo Solution for injection** Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP, live)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you are vaccinated because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your healthcare worker.
- If you get any side effects, talk to your healthcare worker. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What Ervebo is and what it is used for
2. What you need to know before you receive Ervebo
3. How Ervebo is given
4. Possible side effects
5. How to store Ervebo
6. Contents of the pack and other information

#### **1. What Ervebo is and what it is used for**

- Ervebo is a vaccine for adults who are 18 years of age and older.
- Ervebo is given to protect you from getting Ebola virus disease caused by the Zaire Ebola virus, which is a type of Ebola virus. This vaccine will not protect you against the other types of Ebola virus.
- Because Ervebo does not contain the whole Ebola virus, it cannot give you Ebola virus disease.

Your healthcare worker may recommend that you receive this vaccine in an emergency involving the spread of Ebola virus disease.

#### What is Ebola?

- Ebola is a serious disease caused by a virus. If you get Ebola, it can kill you. People catch Ebola from people or animals who are infected with Ebola or who died from Ebola.
- You can catch Ebola from blood and body fluids like urine, stools, saliva, vomit, sweat, breast milk, semen and vaginal fluids of people who are infected with Ebola virus.
- You can also catch Ebola from things that have touched the blood or body fluids of a person or animal with Ebola (like clothes or objects in direct contact).
- Ebola is not spread through the air, water or food.

Your healthcare worker will talk to you and then together you can decide if you should receive this vaccine.

#### **2. What you need to know before you receive Ervebo**

##### **Do not receive Ervebo if you:**

- are allergic to Ervebo, rice, or any of the other ingredients of this vaccine (listed in section 6).
- You should not receive Ervebo if any of the above apply to you. If you are not sure, talk to your healthcare worker.

### **Warnings and precautions**

This vaccine might not protect everyone who receives it and the length of time you are protected from Ebola by Ervebo is not known.

Continue to follow your healthcare worker's recommendations to protect yourself from Ebola infection after you get this vaccine.

Washing your hands correctly is the most effective way to prevent the spread of dangerous germs, like Ebola virus. It reduces the number of germs on the hands and so reduces their spread from person to person.

Proper hand washing methods are described below.

- Use soap and water when hands are soiled with dirt, blood, or other body fluids. There is no need to use antimicrobial soaps for washing hands.
- Use alcohol-based hand sanitiser when hands are not dirty. Do not use alcohol-based hand sanitiser when hands are soiled with dirt, blood, or other body fluids.

While in an area affected by Ebola, it is important to avoid the following:

- Contact with blood and body fluids (such as urine, faeces, saliva, sweat, vomit, breast milk, semen, and vaginal fluids).
- Items that may have come in contact with an infected person's blood or body fluids (such as clothes, bedding, needles, and medical equipment).
- Funeral or burial rituals that require handling the body of someone who died from Ebola.
- Contact with bats, apes and monkeys or with blood, fluids and raw meat prepared from these animals (bushmeat) or meat from an unknown source.
- Contact with semen from a man who had Ebola. You should follow safe sex practices until you know the virus is gone from the semen.

If you get a rash where the skin is broken after receiving Ervebo, cover it until it heals. Put the used plasters and bandages in a sealed container, if possible, and throw them in the waste bin to make sure that people with a weak immune system or animals do not come into contact with the plasters and bandages.

Talk to your healthcare worker before you receive Ervebo if you:

#### Have had allergic reactions to vaccines or medicines

- If you have ever had an allergic reaction to a vaccine or medicine, talk to your healthcare worker before you receive this vaccine.

#### Have a weak immune system

If your immune system is weak (which means your body is less able to fight off diseases), you might not be able to receive Ervebo. You might have a weak immune system if:

- you have HIV infection or AIDS,
- you are taking certain medicines that make your immune system weak such as immunosuppressants or corticosteroids,
- you have cancer or a blood problem that makes your immune system weak,
- a member of your family has a weak immune system.

If you think you might have a weak immune system, ask your healthcare worker if you should receive this vaccine. If you do get the vaccine and have a weak immune system, the vaccine may not work as well as in people with a normal immune system.

#### Are in contact with vulnerable individuals

Tell your healthcare worker if in the 6 weeks after you receive Ervebo you might be in close contact with or in the same household as:

- babies who are less than 1 year old,

- someone who may be pregnant or breast-feeding,
- someone who has a weak immune system.

This is because you could pass on the virus in the vaccine to them through your body fluids.

If you get a rash where the skin is broken after receiving Ervebo, cover it until it heals. Put the used plasters and bandages in a sealed container, if possible, and throw them away in the garbage bin to avoid having people with a weak immune system come into contact with the plasters and bandages.

#### Plan to donate blood

- Do not donate blood for at least 6 weeks after you receive this vaccine.

#### Are in contact with farm animals

- Make sure your blood or body fluids do not come into close contact with farm animals for at least 6 weeks after you receive this vaccine. This is because of a possibility that you could pass on the virus in the vaccine to the animals.
- If you get a rash where the skin is broken after receiving Ervebo, cover it until it heals.
- Put the used plasters and bandages in a sealed container, if possible, and throw them away in the garbage bin to avoid having animals come into contact with the plasters and bandages.

#### Have a fever (high temperature)

- If you have a fever (high temperature), you should talk to your healthcare worker before receiving Ervebo. The vaccination may have to be delayed until your fever is gone.
- A minor infection such as a cold should not be a problem but talk to your healthcare worker before receiving Ervebo.

#### Have a bleeding disorder or bruise easily

- Tell your healthcare worker if you have a problem with bleeding or you bruise easily. Ervebo might make you bleed or bruise where the vaccine is injected.

#### Testing for Ebola after you receive Ervebo

- You may test positive for Ebola virus after you receive Ervebo. This does not mean that you have Ebola. Tell your healthcare worker that you have received Ervebo. Your healthcare worker might need to do another test.

If any of the above warnings and precautions apply to you (or you are not sure), talk to your healthcare worker before receiving Ervebo.

#### **Children and adolescents**

If you or your child is under 18 years old, talk to your healthcare worker. It is not known if it is safe and works in children and adolescents.

#### **Other medicines and Ervebo**

Tell your healthcare worker if you are taking, have recently taken or might take any other medicines or vaccines.

No studies have looked at how other medicines or vaccines and Ervebo might interact with each other. Use of Ervebo with other vaccines is not recommended.

#### If you plan to receive blood or blood products

Do not receive this vaccine at the same time that you get blood or blood products. Ervebo might not work as well if you get blood or blood products 3 months before or up to 1 month after vaccination.

#### **Pregnancy and breast-feeding**

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your healthcare worker for advice before you receive this vaccine. They will help you decide if you should receive Ervebo.

- Do not become pregnant for 2 months after you receive Ervebo. Women who are able to become pregnant should use an effective method of birth control. It is not known if Ervebo will harm you or your unborn baby. It is also not known if it can pass to your baby through your breast milk.
- If you might be in close contact with, or in the same household as someone who may be pregnant or breast-feeding during the 6 weeks after you receive Ervebo, tell your healthcare worker. This is because you could pass the vaccine to them through your body fluids.

### **Ervebo contains sodium**

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

### **3. How Ervebo is given**

Ervebo is given by a healthcare worker. It is given as a single injection (dose of 1 mL) in the top of your arm or the outside of your thigh.

If you have any further questions on the use of this vaccine, ask your healthcare worker.

### **4. Possible side effects**

Like all vaccines, Ervebo can cause side effects, although not everybody gets them.

Serious side effects are rare. Get medical care right away if you have symptoms of an allergic reaction, which may include:

- wheezing or trouble breathing,
- swelling of the face, lips, tongue, or other parts of the body,
- generalized itching, redness, flushing or itchy bumps on the skin.

#### **Other side effects:**

##### **Very common (may affect more than 1 in 10 people):**

- Headache,
- Joint pain,
- Muscle aches,
- Fever,
- Feeling tired,
- Pain, swelling, or redness at the injection site.

##### **Common (may affect up to 1 in 10 people):**

- Stomach pain,
- Nausea,
- Skin rash,
- Joint swelling,
- Chills,
- Excessive sweating.

Certain white blood cell counts can decrease below normal after vaccination but this decrease has not resulted in illness and the counts return to normal.

Most side effects go away within a few days. Joint pain and swelling may last for weeks or months in some people. In some people joint pain and swelling may come back after initially going away.



Tell your healthcare worker if you get any of the side effects listed above.

### **Additional side effects in children and adolescents**

The vaccine has been studied in a small number of children and adolescents who were 6 to 17 years of age. Overall, the side effects in children and adolescents were similar to those in adults.

### **Reporting of side effects**

If you get any side effects, talk to your healthcare worker. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Ervebo**

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the vial label and the outer carton after 'EXP'. The expiry date refers to the last day of that month.
- Store and transport frozen at -80°C to -60°C.
- After thawing, the vaccine should be used immediately. However, once thawed, the vaccine can be stored for up to 14 days at 2°C to 8°C before use. Discard the vaccine if it is not used by the end of 14 days. Once thawed, the vaccine cannot be re-frozen.
- Upon removal from the freezer, the product should be marked with both the date that it was taken out of the freezer and also a new discard date (in place of the labelled expiry date).
- Keep the vial in the outer carton in order to protect from light.
- Do not use this vaccine if you notice particles in the liquid.
- Do not throw away any medicines via wastewater or household waste. Ask your healthcare worker how to throw away medicines you no longer use. These measures will help protect the environment.

## **6. Contents of the pack and other information**

### **What Ervebo contains**

The active substance is a living Vesicular Stomatitis Virus. The surface protein of the virus has been replaced with that of Zaire Ebola Virus (rVSVΔG-ZEBOV-GP).

One dose (1 mL) contains:

Ebola Zaire Vaccine (rVSVΔG-ZEBOV-GP<sup>1,2</sup> live, attenuated) ≥72 million pfu<sup>3</sup>

<sup>1</sup>Recombinant Vesicular Stomatitis Virus (rVSV) strain Indiana with a deletion of the VSV envelope glycoprotein (G) replaced with the Zaire Ebola Virus (ZEBOV) Kikwit 1995 strain surface glycoprotein (GP)

<sup>2</sup>Produced in Vero cells.

<sup>3</sup>pfu= plaque-forming units

This product contains genetically modified organisms (GMOs).

This vaccine contains a trace amount of rice protein.

This vaccine contains less than 1 mmol (23 mg) of sodium per dose.

The other excipients are recombinant human serum albumin, trometamol buffer, water for injections, hydrochloric acid, sodium hydroxide.

### **What Ervebo looks like and contents of the pack**



- Ervebo is a solution for injection.
- Ervebo is a colourless to slightly brownish-yellow liquid.
- Ervebo is available in a pack of 10 vials.

#### **Marketing Authorisation Holder**

Merck Sharp & Dohme B.V.  
 Waarderweg 39  
 2031 BN Haarlem  
 The Netherlands

#### **Manufacturer**

Burgwedel Biotech GmbH  
 Im Langen Felde 5  
 30938 Burgwedel  
 Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

#### **België/Belgique/Belgien**

MSD Belgium BVBA/SPRL  
 Tél/Tel: +32(0)27766211  
 dpoc\_belux@merck.com

#### **Lietuva**

UAB Merck Sharp & Dohme  
 Tel.: +370.5.2780.247  
 msd\_lietuva@merck.com

#### **България**

Мерк Шарп и Доум България ЕООД,  
 тел.: + 359 2 819 3737  
 info-msdbg@merck.com

#### **Luxembourg/Luxemburg**

MSD Belgium BVBA/SPRL  
 Tél/Tel: +32 (0) 27766211  
 dpoc\_belux@merck.com

#### **Česká republika**

Merck Sharp & Dohme s.r.o.  
 Tel.: +420 233 010 111  
 dpoc\_czechslovak@merck.com

#### **Magyarország**

MSD Pharma Hungary Kft.  
 Tel.: + 36.1.888.5300  
 hungary\_msd@merck.com

#### **Danmark**

MSD Danmark ApS  
 Tlf: + 45 4482 4000  
 dkmail@merck.com

#### **Malta**

Merck Sharp & Dohme Cyprus Limited.  
 Tel: 8007 4433 (+356 99917558)  
 malta\_info@merck.com

#### **Deutschland**

MSD SHARP & DOHME GMBH  
 Tel: 0800 673 673 673 (+49 (0) 89 4561 2612)  
 e-mail@msd.de

#### **Nederland**

Merck Sharp & Dohme B.V.  
 Tel: 0800 9999000  
 (+31 23 5153153)  
 medicalinfo.nl@merck.com

#### **Eesti**

Merck Sharp & Dohme OÜ  
 Tel.: +372 6144 200  
 msdeesti@merck.com

#### **Norge**

MSD (Norge) AS  
 Tlf: +47 32 20 73 00  
 msdnorge@msd.no

#### **Ελλάδα**

MSD Α.Φ.Β.Ε.Ε.  
 Τηλ: +30 210 98 97 300  
 dpoc\_greece@merck.com

#### **Österreich**

Merck Sharp & Dohme Ges.m.b.H.  
 Tel: +43 (0) 1 26 044  
 msd-medizin@merck.com

#### **España**

Merck Sharp & Dohme de España, S.A.  
 Tel: +34 91 321 06 00  
 msd\_info@merck.com

#### **Polska**

MSD Polska Sp. z o.o.  
 Tel.: +48.22.549.51.00  
 msdpolska@merck.com

**France**

MSD VACCINS

Tél: +33 (0)1 80 46 40 40

information.medicale@msd.com

**Hrvatska**

Merck Sharp &amp; Dohme d.o.o.

Tel: +385 1 66 11 333

croatia\_info@merck.com

**Ireland**

Merck Sharp &amp; Dohme Ireland (Human Health) Limited

Tel: +353 (0)1 2998700

medinfo\_ireland@merck.com

**Ísland**

Vistor hf.

Sími: + 354 535 7000

**Italia**

MSD Italia S.r.l.

Tel: +39 06 361911

medicalinformation.it@merck.com

**Κύπρος**

Merck Sharp &amp; Dohme Cyprus Limited

Τηλ: 800 00 673 (+357 22866700)

cyprus\_info@merck.com

**Latvija**

SIA Merek Sharp &amp; Dohme Latvija

Tel: +371.67364.224

msd\_lv@merck.com

**Portugal**

Merck Sharp &amp; Dohme, Lda

Tel: +351 21 4465700

inforin\_pt@merck.com

**România**

Merck Sharp &amp; Dohme Romania S.R.L

Tel: + 4021 529 29 00

msdromania@merck.com

**Slovenija**

Merck Sharp &amp; Dohme, inovativna zdravila d.o.o.

Tel: +386.1.520.4201

msd.slovenia@merck.com

**Slovenská republika**

Merck Sharp &amp; Dohme, s. r. o

Tel: +421 2 58282010

dpoc\_czechslovak@merck.com

**Suomi/Finland**

MSD Finland Oy

Puh/Tel: +358 (0)9 804 650

info@msd.fi

**Sverige**

Merck Sharp &amp; Dohme (Sweden) AB

Tel: +46 77 5700488

medicinskinfo@merck.com

**United Kingdom**

Merck Sharp &amp; Dohme Limited

Tel: +44 (0) 1992 467272

medicalinformationuk@merck.com

**This leaflet was last revised in MM/YYYY**

This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.

The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

<----->

The following information is intended for healthcare professionals only:

Standard precautions when caring for patients with known or suspected Ebola disease

Vaccination with Ervebo does not eliminate the necessity of standard precautions when caring for patients with known or suspected Ebola disease. **All healthcare workers, and other ancillary providers who have been vaccinated, should not alter their practices with regard to safe injection, hygiene, and personal protective equipment (PPE) after vaccination.**

Standard precautions, as outlined by WHO, include the following:

- Basic hand hygiene
- Respiratory hygiene
- Use of PPE (to block splashes or other contact with infected materials)
- Safe injection practices
- Safe burial practices

Healthcare workers caring for patients with suspected or confirmed Ebola virus should apply extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding. When in close contact (within 1 metre) of patients with Ebola Virus Disease, healthcare workers should wear face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown, and gloves (sterile gloves for some procedures).

Laboratory workers are also at risk. Samples taken from humans and animals for investigation of Ebola infection should be handled by trained staff and processed in suitably equipped laboratories.

Vaccine administrators should counsel vaccinees to continue to protect themselves with the following measures:

- Hand washing
- Avoid contact with blood and body fluids
- Safe burial practices
- Safe sex
- Avoid contact with bats and non-human primates or blood, fluids and raw meat prepared from these animals (bushmeat) or meat from an unknown source.

#### Instructions on the handling of the vaccine before administration

- Ervebo is stored frozen at -80°C to -60°C and should be removed from the freezer and thawed in less than 4 hours until no visible ice is present. Do not thaw the vial in a refrigerator as it is not guaranteed that the vial will thaw in less than 4 hours. The thawed vial should then be gently inverted several times prior to withdrawal with the syringe.
- After thawing, Ervebo should be used immediately; however, in-use stability data have demonstrated that once thawed, the vaccine can be stored for up to 14 days at 2°C to 8°C prior to use. At the end of 14 days, the vaccine should be used or discarded. Upon removal from the freezer, the product should be marked with both the date that it was taken out of the freezer and also a new discard date (in place of the labelled expiry date). Once thawed, the vaccine cannot be re-frozen.
- Ervebo is a colourless to slightly brownish-yellow liquid. Discard the vaccine if particulates are present.
- Ervebo should be administered intramuscularly. Do not inject the vaccine intravascularly. No data are available for administration via the subcutaneous or intradermal routes.
- Ervebo should not be mixed in the same syringe with any other vaccines or medicinal products.
- Withdraw the entire content of Ervebo from the vial using a sterile needle and syringe. The preferred injection site is the deltoid area of the non-dominant arm or in the higher anterolateral area of the thigh. Cover the injection site with gauze or bandage (e.g. any adhesive bandage or gauze and tape) that provides a physical barrier to protect against direct contact with vesicle fluid. The bandage may be removed when there is no visible fluid leakage.

- Any unused vaccine or waste material should be disposed of in compliance with the institutional guidelines for genetically modified organisms or biohazardous waste, as appropriate. If breakage/spillage were to occur, disinfectants such as aldehydes, alcohols and detergents are proven to reduce viral infection potential after only a few minutes. If feasible, the waste liquid from eye washes should be collected and decontaminated before discarding into the drain.

**From:** Ritchey, Julian /US  
**Sent:** Thu, 5 Dec 2019 21:44:27 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD);Cohn, Amanda (CDC/DDID/NCIRD/OD);Grohskopf, Lisa A. (CDC/DDID/NCIRD/ID);Pope, Kristin (CDC/DDID/NCIRD/OD)  
**Subject:** Influenza EO outreach  
**Attachments:** Dr Robert Kadlec - Letter.pdf

Dear Nancy, et al.

I am reaching out to share a letter we recently sent to Dr. Kadlec to express our support, concerns, and suggestions related to the White House Influenza EO. As follow-up to this communication, we have been reaching out to Task Force stakeholders to share and discuss these thoughts.

We have secured time with Dr Redfield next Tuesday to discuss CDC engagement broadly and I see on the latest planner you have been included. I wanted to both share the context of the meeting and offer to discuss this as a separate group more specific to the key role we hope ACIP will be recognized as playing in any influenza policymaking especially as it regards impacts on seasonal immunization.

The letter is being shared with Dr. Redfield's office shortly as a pre-read for the call. Please let me know if you would be interested in discussing further.

Be well –  
Julian

(b)(4)

(b)(4)

(b)(4)



(b)(4)

**From:** Bresnitz, Eddy A.  
**Sent:** Mon, 9 Dec 2019 02:49:35 +0000  
**To:** Cohn, Amanda (CDC/DDID/NCIRD/OD); Messonnier, Nancy (CDC/DDID/NCIRD/OD); Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD); Rafael Harpaz (b)(6); Strikas, Raymond A. (Ray) (CDC/DDID/NCIRD/ISD); Nelson, Noele (CDC/DDID/NCHHSTP/DVH); Pilishvili, Tamara (CDC/DDID/NCIRD/DBD); Matanock, Almea M. (CDC/DDID/NCIRD/DBD); Craig, Allen (CDC/DDID/NCIRD/DBD); Redd, Stephen (CDC/DDPHSIS/OD); Montero, Jose (CDC/DDPHSIS/CSTLTS/OD); Monroe, Judith A. (CDC/OD/OCS); Pinner, Robert W. (CDC/DDID/NCEZID/OD); Beach, Michael J. (CDC/DDID/NCEZID/DFWED)  
**Cc:** Eddy Bresnitz  
**Subject:** Moving On

Dear CDC Colleagues: I wanted to let you know personally that I will be retiring from Merck on (b)(6). After ~50 years of full-time healthcare-related work and study, from medical school through post-graduate training, patient care, research, education, and public health practice in government and industry, it's time for me to scale back professionally. It's been a real pleasure working with all of you at the CDC on many different issues over the years, dating back to my days in academia (I first met Ray when he was my project officer on a flu/pneu vaccination grant in the mid-90s!) and public health.

I've had a varied and interesting professional life to date, and I view my leaving Merck as the beginning of the next exciting chapter in my life's journey, but no longer working full-time. I do hope to continue to be active in some manner on public health issues, either as a volunteer or as a consultant if the opportunity arises to do something of interest and impact.

Should you wish to contact me in the future, please take note of my personal cell phone number and e-mail address. My Merck contact information will become inactive on (b)(6).

(b)(6) (Home)  
(b)(6) (Cell)

(b)(6)

I hope that we will cross paths again in the not too distant future. I wish you all the best and continued success in the work that you do to protect the public's health.

With best regards,

Eddy

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information

for affiliates is available at  
<http://www.merck.com/contact/contacts.html>) that may be confidential,  
proprietary copyrighted and/or legally privileged. It is intended solely  
for the use of the individual or entity named on this message. If you are  
not the intended recipient, and have received this message in error,  
please notify us immediately by reply e-mail and then delete it from  
your system.

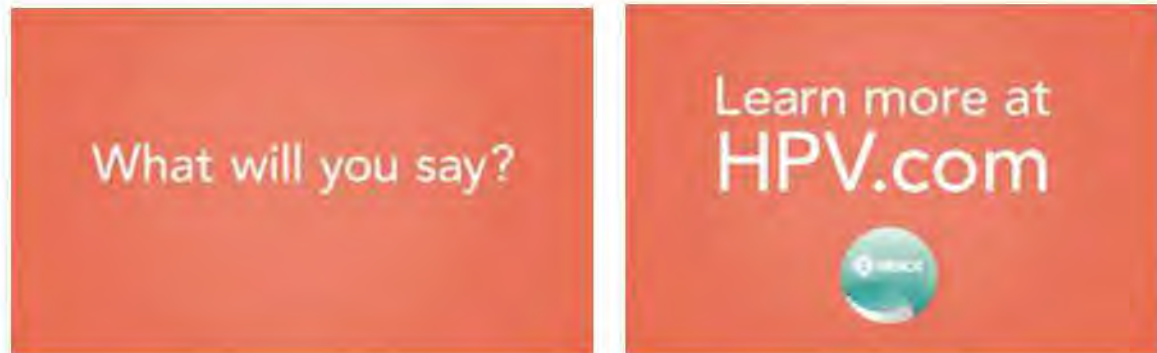
**From:** Kuter, Barbara J.  
**Sent:** Mon, 27 Jun 2016 17:10:43 -0400  
**To:** Markowitz, Lauri (CDC/OID/NCIRD); Wharton, Melinda (CDC/OID/NCIRD); Messonnier, Nancy (CDC/OID/NCIRD)  
**Subject:** New TV Commercial From Merck - HPV

Lauri, Melinda, and Nancy,

I wanted to let you know that beginning in late June 2016, Merck will launch a new TV commercial about human papillomavirus (HPV).

This commercial discusses HPV and its link to certain cancers. Parents are encouraged to ask their children's doctor about HPV and to learn more at [www.HPV.com](http://www.HPV.com).

We welcome you to preview the full 60-second commercial at [www.hpvtvad.com](http://www.hpvtvad.com).



[Click here to watch the TV commercial](#)

I would appreciate if you would not distribute this outside of CDC.

Thanks.

Barb



Copyright © 2016 Merck Sharp & Dohme Corp., a subsidiary of **Merck & Co., Inc.** All rights reserved.  
VACC-1183440-0004 06/16

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information

for affiliates is available at  
<http://www.merck.com/contact/contacts.html>) that may be confidential,  
proprietary copyrighted and/or legally privileged. It is intended solely  
for the use of the individual or entity named on this message. If you are  
not the intended recipient, and have received this message in error,  
please notify us immediately by reply e-mail and then delete it from  
your system.

**From:** Grabenstein, John D.  
**Sent:** Fri, 20 Oct 2017 16:09:26 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Cohn, Amanda (CDC/OID/NCIRD)  
**Subject:** FW: Draft slides in advance of ACIP

Nancy,

Eddy's e-mail to Kathleen accurately reflects the reaction of our scientists.

(b)(4)

(b)(4)

John

---

**From:** Bresnitz, Eddy A.  
**Sent:** Thursday, October 19, 2017 16:58  
**To:** Dooling, Kathleen L. (CDC/OID/NCIRD)  
**Cc:** Harpaz, Rafael (CDC/OID/NCIRD); Patel, Manisha M. (CDC/OID/NCIRD); Guo, Angela (CDC/OID/NCIRD); Draghia, Ruxandra; Grabenstein, John D.; Cohn, Amanda (CDC/OID/NCIRD); Nancy Messonnier (nar5@cdc.gov); Roberts, Craig  
**Subject:** Draft slides in advance of ACIP

**Proprietary**

Dear Kathleen: We have reviewed the CDC model developed by Dr. Prosser as well as the policy considerations.

(b)(4)

(b)(4)

(b)(4)

Thank you again for the opportunity to review the presentations in advance of next week's meeting. If you wish to discuss this further, don't hesitate to call.

Best, Eddy

Eddy Bresnitz, MD, MSCE  
Executive Director, Adult Vaccines  
Global Vaccines Medical Affairs  
Merck Vaccines

351 N. Sumneytown Pike  
North Wales, PA 19454

(b)(6)

---

**From:** Dooling, Kathleen L. (CDC/OID/NCIRD) [<mailto:vic9@cdc.gov>]

**Sent:** Wednesday, October 18, 2017 2:27 PM

**To:** Bresnitz, Eddy A.

**Cc:** Harpaz, Rafael (CDC/OID/NCIRD); Patel, Manisha M. (CDC/OID/NCIRD); Guo, Angela (CDC/OID/NCIRD)

**Subject:** Draft slides in advance of ACIP

Hello Eddy,

Please find attached the draft slides for the Health Economic presentation and the Policy Considerations presentation.

Please consider these slides as draft and subject to change prior to the ACIP meeting. Also, we ask that you consider these slides confidential.

Please let us know if there are any errors in the data pertaining to Zostavax.

Sincerely,  
Kathleen

Dr. Kathleen Dooling MD MPH  
Medical Officer  
Centers for Disease Control and Prevention  
Measles Mumps Rubella Herpes Polio Team

[Vic9@cdc.gov](mailto:Vic9@cdc.gov)

Office Phone: 404-718-1174

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.



**From:** Barbara Howe  
**Sent:** Mon, 14 Mar 2016 20:32:06 +0000  
**To:** Messonnier, Nancy (CDC/OID/NCIRD)  
**Cc:** Leonard Friedland  
**Subject:** NCIRD Leadership Announcement

Dear Nancy

On behalf of GSK, we would like to take this opportunity to congratulate you on your appointment to Director of the National Center for Immunization and Respiratory Diseases (NCIRD).

We very much appreciate your approach to open dialogue and provision of feedback over the years and we look forward to continuing to work with CDC on efforts to reduce vaccine-preventable diseases in the US and globally.

Sincerely

Barbara and Len

**Barbara J. Howe, MD**  
**Vice President and Director**  
**Vaccines Clinical and Medical, US**

**Leonard Friedland, MD**  
**Vice President, Scientific Affairs and Public Health**  
**Vaccines, US**

**GSK**  
**S Crescent Drive, Philadelphia, PA 19112**

**From:** Thomas R. Frieden (CDC)  
**Sent:** Monday, March 14, 2016 9:32 AM  
**To:** CDC All - CDC & ATSDR and non-CDC & non-ATSDR <[allcdcwide@cdc.gov](mailto:allcdcwide@cdc.gov)>  
**Subject:** Leadership Announcement

I am pleased to announce that Dr. Nancy Messonnier (CAPT, USPHS) has accepted the position of director of the National Center for Immunization and Respiratory Diseases (NCIRD). Nancy has served as NCIRD deputy director since October 2014, helping lead the Center through various high-profile challenges including the 2015 US measles outbreak, ongoing domestic and

global respiratory disease outbreaks, Global Health Security Agenda activities, implementation of Ebola vaccine trials, and the latest actions toward polio eradication.

Nancy received her BA from the University of Pennsylvania and MD from the University of Chicago School of Medicine, and completed internal medicine residency training at the University of Pennsylvania. She joined CDC in 1995 as an Epidemic Intelligence Service (EIS) officer in the Childhood and Respiratory Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases. Following EIS, she joined the division's Meningitis and Special Pathogens Branch, where she held ongoing leadership positions, becoming branch chief in 2005 and continuing as chief of the Meningitis and Vaccine-Preventable Disease Branch in NCIRD from the Center's formation in 2006 through 2012. Additional leadership positions since 2012 include interim director of the Advanced Molecular Detection Implementation team in the National Center for Emerging and Zoonotic Diseases (NCEZID), acting deputy director of the Center for Surveillance, Epidemiology and Laboratory Services (CSELS), and acting director of the Division of Global Health Protection in the Center for Global Health.

Nancy has played critical roles in many efforts to reduce vaccine-preventable diseases, including the highly successful public-private partnership to develop and implement a low-cost vaccine (MenAfriNet) to prevent epidemic meningococcal meningitis in Africa. She has also worked tirelessly to prevent and control bacterial meningitis in the United States, including drafting the initial recommendations for use of meningococcal polysaccharide vaccine in young adults heading for college. She also oversaw a family of studies exploring the US resurgence of pertussis and characterizing post-licensure effectiveness of acellular pertussis vaccines. A well-recognized expert in *Bacillus anthracis*, Nancy served in leadership roles during the public health response to the 2001 intentional anthrax release, has served as co-leader of the anthrax management team and vaccine working group, and served as incident commander as part of the agency's response to the 2014 CDC anthrax laboratory incident.

I would also like to thank CDC Deputy Director for Infectious Diseases and Director of the Office of Infectious Diseases, Rima Khabbaz, PhD, for her outstanding leadership of NCIRD over the last 6 months during our search for a new permanent NCIRD director. Nancy will begin her new position on April 4. Please join me in supporting her in this new role and in thanking Rima for her dedication and many contributions.

Thomas R. Frieden, MD, MPH  
Director, CDC, and  
Administrator, ATSDR

**From:** (b)(6)  
**Sent:** Thu, 19 Apr 2018 19:16:41 +0000  
**To:** (b)(6); baltimo@caltech.edu; Messonnier, Nancy (CDC/OID/NCIRD); (b)(6)  
**Cc:** (b)(6); catharine.paules@nih.gov; Conrad, Patricia (NIH/NIAID) [E]; Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Final submission attached

Thank you for your time and effort, not to mention the work by David, Tony and Nancy.  
I look forward hearing further and hope we are able to do the session.  
Best  
Gary

---

**From:** Chandross, Karen /US  
**Sent:** Thursday, April 19, 2018 1:53 PM  
**To:** Baltimore, David; Messonnier, Nancy (CDC/OID/NCIRD); anthony.fauci@nih.gov; Nabel, Gary /US  
**Cc:** Wei, Ronnie /US; Travayiakis, Carol /US; Paules, Catharine (NIH/NIAID) [E]; Conrad, Patricia (NIH/NIAID) [E]; Cozart, Barbara (CDC/OID/NCIRD)  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal -- Final submission attached

Final submission attached for your records.

I spoke to Bill Beck, the Pharmaceutical Sciences Section Secretary -- and he has agreed to endorse our submission.

Thank you!  
Karen

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL: (b)(6) (b)(6)

---

**From:** Chandross, Karen /US  
**Sent:** Monday, April 16, 2018 11:16 AM  
**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov> (b)(6)  
(b)(6); Nabel, Gary /US (b)(6)  
**Cc:** 'Baltimore, David' <baltimo@caltech.edu>; Wei, Ronnie /US (b)(6)  
Travayiakis, Carol /US (b)(6); 'Conrad, Patricia (NIH/NIAID) [E]' <conradpa@niaid.nih.gov>; Cozart, Barbara (CDC/OID/NCIRD) <wjn4@cdc.gov>  
**Subject:** RE: AAAS 2019 -- Universal flu vaccine proposal invitation -- all proposed participants confirmed -- please send title & 2-3 sentence description  
**Importance:** High

Dear All – thank you for agreeing to participate in a proposed 2019 AAAS session, which focuses on addressing *The quest for a universal flu vaccine*.

We are very excited to have a great line up and, if selected, David Baltimore has kindly agreed to serve as moderator.

Speakers:

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

Keeping in mind the April 19<sup>th</sup> submission deadline, for our speakers, I must submit a 1) a **title for your talk** and 2) **up to 3 short sentences that describes your focus**-- if you would send this to me at your earlier convenience.

Please note that we would plan to have short talks followed by a longer panel discussion that also includes engaging the audience.

All the best,  
Karen

**Info:**

1. 2019 AAAS meeting (February 14-18) in Washington, DC.
2. In line with AAAS's interest in topics with broad appeal and relevancy, we are submitting a proposal for a 90-min symposium (<https://aaas.confex.com/aaas/2019/symp90/cfp.cgi>) on "*The quest for a universal flu vaccine*."
3. Theme is "*Science Transcending Boundaries*," which offers an opportunity to bridge the gap between scholar and practitioner and leverage expertise from different disciplines to highlight the greatest challenges and most promising solutions to achieving an impactful solution.
4. For the session format, 3 speakers are asked to give presentations (~20 minutes each), followed by a ~30 minute Q&A period with the audience.

**The quest for a universal flu vaccine**

According to the World Health Organization, seasonal influenza epidemics cause 3 to 5 million severe cases and 300,000 to 500,000 deaths globally each year. In the United States alone, there are 140,000 to 710,000 influenza-related hospitalizations and 12,000 to 56,000 deaths each year, with the highest burden of disease affecting the very young, the very old, and people with coexisting medical conditions. The most recent 2017/2018 seasonal vaccine has a 36% overall effectiveness rate in preventing influenza. This modest outcome is typical and may be due in part to strain mutations, immune evasion through antigenic drift, immune waning with time, and, perhaps, egg-adapted viral mutations. There has been an infusion of new scientific insights and technologies but little improvement in influenza prevention or epidemic control, suggesting that its eradication will require a paradigm shift in how we approach research, development and global access. Questions remain, such as whether targeting more

conserved viral regions or utilizing cell-based, chimeric or recombinant technologies will bring about improvements. Or whether more focus should be placed on development, including the development of better predictive models and biomarkers that combine data from patient-centered devices, sensors and clinical measurements to stay abreast of surveillance and better forecasts which strains are likely to predominate in the coming season. This session will bridge the gap between scholar and practitioner and leverage expertise from a variety of disciplines to highlight the greatest challenges and most promising solutions to achieving a universal flu vaccine that is durable across all populations. Short talks will be followed by a panel discussion where the moderator will challenge the proposals and engage the audience.

**Moderator:** David Baltimore, PhD

**Speakers:**

Gary Nabel, MD, PhD, Sanofi CSO

Anthony Fauci, MD, NIH-NIAID Director

Nancy Messonnier, MD, CDC-NCIRD Director

**Organizer:** Karen Chandross, PhD, Sanofi R&D

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL: (b)(6) (b)(6)

**From:** (b)(6)  
**Sent:** Thu, 17 Jan 2019 18:16:28 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Cozart, Barbara (CDC/DDID/NCIRD/OD); anthony.fauci@nih.gov; Conrad, Patricia (NIH/NIAID) [E]; (b)(6)  
**Cc:** baltimo@caltech.edu; ktclark@caltech.edu  
**Subject:** RE: 2019 AAAS Annual Meeting -- Flu Session Feb 16, 2019 -- Session planning update for your input

Dear Tony, Gary and Nancy,

After speaking to David, we would like to share a more detailed proposal for our 90 min flu session/panel discussion aimed at maximizing your time and reducing overlap.

In order of presentation:

1. David (10 min) can set the stage for how influenza virus gets into body, infects cells and causes the flu. He can then summarize the current state of vaccines as ineffective/inconsistent preventative measures, mention the key challenges to achieving a universal/broadly protective flu vaccine and summarize the unmet needs. This would be a very high level overview with graphics.
2. Tony (15 min + 5 min Q&A) can go into detail around the major challenges to achieving a universal/broadly protective vaccine, highlight some of the low-hanging opportunities (scientific, production, regulation), describe some of the most exciting enablers and exemplify how we are working across sectors/disciplines to achieve common ground to deliver.
3. Gary (15 min + 5 min Q&A) can go into detail around alternative paths to achieving a universal/broadly protective influenza therapies/vaccines, prototypic vaccines, proof of principle studies, opportunities for challenge models, the key challenges and potential solutions, and what it takes to go from scientific proof of principle through clinical trials.
4. Nancy (15 min + 5 min Q&A) can summarize how the NCIRD-CDC currently operates and envisions adapting to a UFV and can go into detail around new technologies/innovations and big data/AI approaches being employed to reduce the burden until a UFV is achieved and, in general, can be used to predict strains and sources, track vaccine efficacy, provide surveillance and enable global readiness.
5. (20 min) Panel discussion with all speakers (David to moderate) that includes 2-3 pre-set questions and then is open to the audience.

Please let us know your thoughts or would like to cover something that is not captured – keeping in mind that we are trying to keep the talks shorter in order to allow for a stimulating panel discussion.

We'll share thoughts for the panel discussion topics soon for your input.

Once you have your near-ready slide decks, please share these with David to help in organizing his introduction.

Also, if you have a favorite graphic or short video clip he can use, please let us know.

As a reminder, our



- News Briefing is on Feb 16<sup>th</sup> at 10 am at Balcony A in the Marriott Wardman Park Hotel, Washington, DC.
- Flu session is on Feb 16<sup>th</sup> from 3:30 – 5 pm at the Wardman, with the room to be confirmed within the next 2 weeks.  
We can expect up to 150 senior scientists and policymakers, as well as students, K-12 teachers, science advocates, and members of the media.

Thank you!  
Karen

**Karen CHANDROSS, PhD**

Sanofi R&D

TEL: (b)(6) CELL (b)(6) (b)(6)

**From:** Chandross, Karen /US

**Sent:** Wednesday, December 5, 2018 1:53 PM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <nar5@cdc.gov>; 'Cozart, Barbara (CDC/OID/NCIRD)' <wjn4@cdc.gov>; (b)(6) Conrad, Patricia (NIH/NIAID) [E] <conradpa@niaid.nih.gov>; Nabel, Gary /US (b)(6); Travayiakis, Carol /US (b)(6) Wei, Ronnie /US (b)(6)

**Cc:** 'Baltimore, David' <baltimo@caltech.edu>

**Subject:** RE: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

You each should have received an email from AAAS requesting abstracts for your individual talks. I had included short abstracts in our original submission from which you can work from -- and have attached these for your convenience (see below for extractions).

Amanda Johnson, communications lead for AAAS, has **Nancy Messonnier, Anthony Fauci and Gary Nabel listed as participating in a news briefing** and she should be coordinating the timing for this directly with you. Gary, Amanda confirmed with John Shiver that he will join you for the briefing.

AAAS is also asking that you **upload your slide presentations by mid-January** since these will be used as a foundation to frame the news briefing.

As a reminder, we will have shorter talks with a panel discussion at the end. For planning, since there is 90 min total for 3 speakers and a short introduction by David Baltimore—this means about 5 min introduction, 20 min for each talk and then 25 min for the panel and Q&A, moderated by David Baltimore. Let me know if you have another suggestion.

Wishing you happy holidays.

Best,  
Karen

**Gary Nabel****Title:** Rational Design and Development of Universal Influenza Vaccines**Summary:** This talk will cover the alternative paths to improved influenza vaccines. Different potential approaches to a broadly protective antibody will be highlighted. Major scientific challenges and opportunities based on influenza biology and the human immune response will be discussed. Finally, considerations for product development will be reviewed, including clinical testing, regulatory, and manufacturing issues, as well as opportunities to advance through public-private partnerships.**Anthony Fauci****Title:** Chasing Influenza: The Need for a Universal Influenza Vaccine**Summary:** Strain-specific vaccination for influenza is suboptimal: 1) Seasonal vaccines are not consistently effective 2) Pandemics occur and response after the fact is ineffective 3) chasing after potential pandemic viruses is costly and ineffective. Our goal is a universal influenza vaccine that would protect against both seasonal and pandemic viruses. To achieve this, we must improve production strategies for influenza vaccines and advance from strain-specific to universal strain coverage.**Nancy Messonnier****Title:** Hit me with your best shot: before and after a universal flu vaccine**Summary:** While the promise of a universal flu vaccine may be years in the future, how can we reduce flu's burden until one is developed and what ground work can we lay in advance? As we track domestic and international surveillance trends and learn more about how flu works and our response to it, we have to improve our current vaccines and evaluate if different types of vaccine are more beneficial. Data tells us that flu vaccine coverage is linked to how well the vaccine works. Working to ensure the current vaccines are effective and safe before we have a universal vaccine can pave the way for its acceptance.

---

**From:** Chandross, Karen /US**Sent:** Thursday, November 29, 2018 8:08 AM**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <[nar5@cdc.gov](mailto:nar5@cdc.gov)>; 'Cozart, Barbara (CDC/OID/NCIRD)' <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>; 'anthony.fauci@nih.gov' <(b)(6)>; 'Conrad, Patricia (NIH/NIAID) [E]' <[conradpa@niaid.nih.gov](mailto:conradpa@niaid.nih.gov)>; 'Baltimore, David' <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; Nabel, Gary /US

(b)(6) Travayiakis, Carol /US &lt;(b)(6)&gt; Wei, Ronnie /US

(b)(6)

**Subject:** RE: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

Dear Colleagues,

You may have received an email from AAAS specifying your time slot for our flu session – please let me know if this is not the case.



We are confirmed for Saturday, February 16, 2019 (3:30 – 5 pm) – hoping that you can stay for the entire session.

As a reminder, if you agreed to meet with Amanda Johnson ([abjohnson@aaas.org](mailto:abjohnson@aaas.org)), AAAS' Press Deputy Director, in a press conference to highlight cutting edge science coming out of your research labs before our session, please consider this in your travel plans. As previously mentioned, I had suggested a group interview (if feasible) around ways of working together to solve some of the biggest challenges to achieving broadly protective or universal vaccines. I will follow up around where this stands.

I'll reach out again with any updates before the winter holidays.

Best regards,  
Karen

**From:** Chandross, Karen /US

**Sent:** Monday, October 1, 2018 1:28 PM

**To:** 'Messonnier, Nancy (CDC/OID/NCIRD)' <[nar5@cdc.gov](mailto:nar5@cdc.gov)>; 'Cozart, Barbara (CDC/OID/NCIRD)' <[wjn4@cdc.gov](mailto:wjn4@cdc.gov)>; (b)(6) 'Conrad, Patricia (NIH/NIAID) [E]' <[conradpa@niaid.nih.gov](mailto:conradpa@niaid.nih.gov)>; 'Baltimore, David' <[baltimo@caltech.edu](mailto:baltimo@caltech.edu)>; Nabel, Gary /US (b)(6) Travayiakis, Carol /US (b)(6) Wei, Ronnie /US

**Subject:** FW: [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule -- Flu Session Feb 16, 2019

Dear Colleagues,

Our **flu vaccine session is confirmed for Saturday, February 16, 2019 (3:30 – 5 pm)** – if you would be please block your calendars, register for the meeting and finalize your travel arrangements as soon as possible.

You should have received the registration link (which then also opens up hotel registration) directly from the AAAS. If this is not the case, please reach out to Ashira Greene ([agreene@aaas.org](mailto:agreene@aaas.org)) directly.

You may have been contacted by Amanda Johnson, AAAS' Press Deputy Director. She would like to highlight cutting edge science coming out of your research labs in a press conference, to be held before our session – so please consider this when planning your travel. I had suggested that since this session involves very senior level experts from across the different healthcare sectors, it could be interesting to engage the panel (together) around ways of working together to solve some of the biggest challenges to achieving broadly protective or universal vaccines.

Thank you.  
Karen

**From:** [aaas@confex.com](mailto:aaas@confex.com) [<mailto:aaas@confex.com>]

**Sent:** Monday, October 1, 2018 11:58 AM

**To:** Chandross, Karen /US (b)(6)

**Subject:** [EXTERNAL] 2019 AAAS Annual Meeting - Your Session Schedule



Dear Karen Chandross, PhD,

Your session at the 2019 AAAS Annual Meeting in Washington, DC has been scheduled.

Title: The Quest for a Universal Flu Vaccine

Date: Saturday, February 16, 2019

Time: 3:30 PM to 5:00 PM

Scheduling took many variables into consideration, including speaker and organizer conflicts. The schedule is final and additional changes are unable to be accommodated. If an emergency arises, please contact me. If you are organizing more than one session, you will receive a separate email for each one.

Please inform the participants in your session(s). Organizers are responsible to disseminate this and other relevant information to all participants in their panels.

The room will be equipped with an LCD projector and screen, a laptop, a head table for three, one podium microphone, and one table microphone, which will be billed to AAAS. Shared Wi-Fi will be available in the meeting rooms. The addition of extra equipment, such as a wired Internet connection, presentation remote, or additional microphones is your responsibility and will not be billed to AAAS. To order additional equipment at your cost, a list of vendors will be available on your [Participant Page](#) in late January. This [page](#) will be updated several times before February with logistical information, tools, and tips for your use in preparing your presentation.

Starting in late December, AAAS will poll registrants as to which sessions they are most interested in attending. Once the results are in, the room assignments will be determined and published in late January. Poll results will strongly affect but not be the only determining factor in room assignments.

For more information about the 2019 AAAS Annual Meeting, visit [www.aaas.org/meetings](http://www.aaas.org/meetings). The meeting schedule will be available online Tuesday, October 9, 2018. Meeting registration is open; all confirmed

speakers have received registration instructions by email. If you have questions about how to register, please email [meetings@aaas.org](mailto:meetings@aaas.org).

If you must withdraw your session, make a presenter change, or have questions about your session, please contact me as soon as possible at [agreene@aaas.org](mailto:agreene@aaas.org) or (202) 326-6593.

Sincerely,  
Ashira

**Ashira B. Greene, Ph.D.**

Program Associate, Office of Meetings and Special Events  
American Association for the Advancement of Science  
1200 New York Avenue NW  
Washington, DC 20005  
P: 202-326-6593  
E: [agreene@aaas.org](mailto:agreene@aaas.org)

**AAAS Annual Meeting**

February 14-17, 2019 • Washington, DC  
[www.aaas.org/meetings](http://www.aaas.org/meetings)

**From:** Hering, David  
**Sent:** Thu, 9 Jan 2020 16:39:27 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD);Cohn, Amanda (CDC/DDID/NCIRD/OD)  
**Cc:** Aleshire, Noah (CDC/DDID/NCIRD/OD);Cane, Alejandro;Forte, Caroline;Coen, Lisa  
**Subject:** Clarification on Pfizer Private Vaccine Price Increases

Dear Nancy and Amanda – I hope you had a pleasant holiday. I wanted to touch base following our helpful meeting in October following the last ACIP meeting. My team and I are grateful for this effort to reset our relationship and appreciate the continued collaboration in recent months.

(b)(4)

In leading our North American commercial work, I am very sensitive to the U.S. environment on drug pricing. My colleagues and I have given careful consideration to our approach and implementation of price changes to mitigate impact to U.S. patients and physicians. The increase this year is due to inflation and our continuing strong investment to develop and manufacture the next generation of vaccines.

I hope this information is useful. Please let me or my team know if you have any questions. Thank you again.

Best regards,  
Dave

David Hering  
Regional President North America Vaccines  
Tel (b)(6)  
Mob

**From:** Ritchey, Julian /US  
**Sent:** Tue, 18 Feb 2020 14:03:49 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD);Grohskopf, Lisa A. (CDC/DDID/NCIRD/ID);Cohn, Amanda (CDC/DDID/NCIRD/OD);Pope, Kristin (CDC/DDID/NCIRD/OD)  
**Subject:** Head's up on Sanofi / HHS coronavirus collaboration  
**Attachments:** Sanofi Coronavirus Partnership[2].pdf

Dears -

I'm reaching out to provide you advance news of an announcement we will be making today regarding our engagement with BARDA to advance a new vaccine against COVID-19 using our (b)(4)

(b)(4)

Please see the attached press release which will be made public at 10am ET today. I'm sharing this in advance with you for your awareness and information asking that you not publicize or distribute the information or release until after 10am ET.

I'd be interested to know any questions or thoughts you have on this and look forward to seeing you at ACIP next week.

Julian



## **Sanofi joins forces with U.S. Department of Health and Human Services to advance a novel coronavirus vaccine**

- \* Work with Biomedical Advanced Research and Development Authority (BARDA) will utilize Sanofi's well-established recombinant technology platform to expedite a potential COVID-19 vaccine

**PARIS – February 18, 2020** – Sanofi Pasteur, the vaccines global business unit of Sanofi, will leverage previous development work for a SARS vaccine which may unlock a fast path forward for developing a COVID-19 vaccine. Sanofi will collaborate with the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response, expanding the company's long-standing partnership with BARDA.

COVID-19 belongs to a family of coronaviruses that can cause respiratory disease. In late 2002, the SARS (severe acute respiratory syndrome) coronavirus emerged and then largely disappeared by 2004. Sanofi plans to further investigate an advanced pre-clinical SARS vaccine candidate that could protect against COVID-19.

*"Addressing a global health threat such as this newest coronavirus is going to take a collaborative effort, which is why we are working with BARDA to quickly advance a potential vaccine candidate," said David Loew, Global Head of Vaccines at Sanofi. "While we are lending our expertise where possible, we believe the collaboration with BARDA may provide the most meaningful results in protecting the public from this latest outbreak."*

### **Sanofi to utilize innovative recombinant technology platform**

Sanofi will use its recombinant DNA platform to produce a 2019 novel coronavirus vaccine candidate. The recombinant technology produces an exact genetic match to proteins found on the surface of the virus. The DNA sequence encoding this antigen will be combined into the DNA of the baculovirus expression platform, the basis of Sanofi's licensed recombinant influenza product, and used to rapidly produce large quantities of the coronavirus antigen which will be formulated to stimulate the immune system to protect against the virus.

*"Emerging global health threats like the 2019 novel coronavirus require a rapid response," said BARDA Director Rick A. Bright, Ph.D. "By expanding our partnership with Sanofi Pasteur and leveraging a licensed recombinant vaccine platform, we hope to speed development of a vaccine candidate to protect against a new virus."*



## Sanofi uniquely positioned in search for a coronavirus vaccine

In non-clinical studies, the SARS vaccine candidate was immunogenic and afforded partial protection as assessed in animal challenge models. This development work by Protein Sciences (acquired by Sanofi in 2017) provides a head start in expediting a COVID-19 vaccine. Additionally, since there is a licensed vaccine based on this platform this will allow for research and materials to be produced relatively quickly for clinical testing. Sanofi's platform also has the potential to manufacture large quantities of the vaccine candidate.

## Sanofi's long-standing commitment to protecting public health

This agreement with BARDA marks another milestone in Sanofi's ongoing contributions to help fight public health threats. Sanofi continues to actively explore potential opportunities where the company's deep vaccine experience and innovative technologies may contribute to addressing the coronavirus public health situation, including sharing Sanofi's vaccine research and development experience with the Coalition for Epidemic Preparedness Innovations.

In December 2019, Sanofi also entered into [an agreement with BARDA](#) to establish state of the art facilities in the U.S. for the sustainable production of an adjuvanted recombinant vaccine for use in the event of an influenza pandemic and based on the same technology platform that will be used for the COVID-19 program.

### About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

Sanofi, Empowering Life

### Media Relations Contact

Marion Breyer

Tel.: +33 (0)1 53 77 46 46

[mr@sanofi.com](mailto:mr@sanofi.com)

### Investor Relations Contact

Felix Lauscher

Tel.: +33 (0)1 53 77 45 45

[ir@sanofi.com](mailto:ir@sanofi.com)

### Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified

by the words “expects”, “anticipates”, “believes”, “intends”, “estimates”, “plans” and similar expressions. Although Sanofi’s management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi’s ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic conditions, the impact of cost containment initiatives and subsequent changes thereto, the average number of shares outstanding as well as those discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under “Risk Factors” and “Cautionary Statement Regarding Forward-Looking Statements” in Sanofi’s annual report on Form 20-F for the year ended December 31, 2018. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.



**From:** Macareo, Louis Robert  
**Sent:** Thu, 27 Feb 2020 03:32:16 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** Thank you [Confidential]

**Confidential**

Nancy,

I work with Beth-Ann Collier at Merck and was at the meeting today. Applause aside, I wanted to take the opportunity to thank you for your work on the Coronavirus situation. I know that everything at CDC is a team effort, but you deserve credit both as the representative head and for your individual effort. There have been budget difficulties and then this virus dropped in your lap. I have rarely been so proud of my government when I see public servants like yourself and everyone at CDC taking such a leadership role and inspiring confidence in the American people about our nation's response. Please know that everyone supports you... maybe millions that will not know you or understand what happens at CDC, but they are grateful as well. Please keep up the good work. I wish you all strength and stamina possible. Take care.

Sincerely,

Louis

Louis Macareo, MD, JD, MPH  
Executive Director, New Diseases Vaccines Lead  
Global Medical Affairs  
Merck Research Labs, Merck & Co., Inc.

(b)(6)  
Office: (b)(6)

Notice: This e-mail message, together with any attachments, contains information of Merck & Co., Inc. (2000 Galloping Hill Road, Kenilworth, New Jersey, USA 07033), and/or its affiliates. Direct contact information for affiliates is available at <http://www.merck.com/contact/contacts.html>) that may be confidential, proprietary, copyrighted and/or legally privileged. It is intended solely for the use of the individual or entity named on this message. If you are not the intended recipient, and have received this message in error, please notify us immediately by reply e-mail and then delete it from your system.

**From:** Ritchey, Julian /US  
**Sent:** Sat, 28 Mar 2020 18:25:21 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD);Cohn, Amanda (CDC/DDID/NCIRD/OD);Grohskopf, Lisa A. (CDC/DDID/NCIRD/ID)  
**Subject:** Sanofi and Translate Bio COVID-19 Collaboration Announcement

Dears –

Sharing the following to keep you informed of our latest effort in the fight against COVID-19. This is a second vaccine initiative for Sanofi Pasteur and additive to the therapeutic efforts going on through our Sanofi parent company related to sarilumab and hydroxychloroquine.

<http://www.news.sanofi.us/2020-03-27-Sanofi-and-Translate-Bio-collaborate-to-develop-novel-mRNA-vaccine-candidate-against-COVID-19>

On a more personal note...

I hope this finds you and your families well.

Thank you for your determination and resolve to follow the science versus the rhetoric in guiding the country through these unprecedented times. Though it may not always seem like it, most of us are very grateful for your work...and eventually, the rest of us will be.

Please let me / us know anything we can do to help –

Julian

**From:** Ritchey, Julian /US  
**Sent:** Fri, 26 Jun 2020 03:38:30 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** Appreciation and support

Dear Nancy –

Following yesterday's ACIP meeting, I wanted to send you a note to say that I truly appreciated your comments and recognition of the issues of diversity. Succinct and well-stated, it made all (certainly me) think about how we approach the challenges in front of us to vaccine access and social disparities, but also how we operate as organizations to insure diversity. Thank you for making that bold effort to address this very topical and all too prevalent issue.

On a very different note, I was taken-aback by the discussion during the meeting regarding the role of ACIP in the COVID vaccine response. To hear that OWS would be interested to "take ACIP's input" and "work with you" felt neither reassuring nor respectful of the ACIP's longstanding role in vaccine policy-setting for the US.

Given the concerns we hear already related to public perception amid the expedited SAR-CoV-2 development process, and the myriad challenges to successful local implementation, my colleagues and I at Sanofi Pasteur certainly feel ACIP needs to be the recommending body for any new vaccine. The practical experience in all things vaccine, the strong public health focus, and most of all, its depth of expertise all make it the natural choice.

Is there something we at Sanofi Pasteur (and/or more broadly through BIO), do to support the direct and primary engagement of ACIP in the COVID-19 immunization guidance and roll-out?

Again, well done to you and the team for successfully producing the first virtual ACIP.

Sincerely,  
Julian Ritchey

**From:** Cane, Alejandro  
**Sent:** Sat, 29 Aug 2020 14:08:50 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Subject:** COVID 19 Vaccine Pfizer candidate

Dear Nancy,  
I hope you and your family are all doing well.

First of all, my apologies to bother you with another email. I know it is an unimaginably busy time for you and your team but considering our COVID 19 vaccine candidate's clinical program is advancing and the challenges that its implementation could represent, I wanted to ask for a short phone call to update you about it and how we can collaborate with you and your team in the near future.

Secondly, I wanted to thank you for the contact with Kim Fox and Melinda Wharton, as probably you are aware, we have had a very good meeting couple of months ago.

Finally, we are very grateful for the time and assistance of ACIP people leading different work groups, we are interacting with. In view of the COVID-19 pandemic and to provide broader protection against pneumonia, (b)(4)

(b)(4) We have had some excellent informational calls with the pneumococcal work group leads on this and we are very thankful for their time. I know how incredibly busy you are but I was hoping you might have a few minutes to spare to speak with me on these topics.

Thanks in advance for your time.

Best regards,  
Alejandro

Alejandro Cané, MD PhD  
North America Vaccines Medical and Scientific Affairs Lead  
Pfizer Biopharmaceuticals Group  
Complejo Thames Office Park  
Colectora Panamericana 1804, 1 Piso Sector "B" Lado Sur  
Villa Adelina (CP 1607EEV) Pcia Buenos Aires-Argentina  
Tel: (b)(6)  
Mobile (b)(6)  
e mail: (b)(6)



**From:** Ritchey, Julian /US  
**Sent:** Wed, 16 Sep 2020 21:02:17 +0000  
**To:** Wharton, Melinda (CDC/DDID/NCIRD/ISD);Messonnier, Nancy (CDC/DDID/NCIRD/OD);Santoli, Jeanne (CDC/DDID/NCIRD/ISD)  
**Cc:** Binder, Tami /US  
**Subject:** Updated State Claims Data  
**Attachments:** State Claims\_External Parties 09082020[2].pptx, IQVIA Claims Variance Tracker 09082020[2].xlsx

Dear all–

Updated data continuing the perspective sharing on routine vaccination rates based on claims data (or sales in the case of the IQVIA summary slide)

Also sharing another file that tracks the data over time so we can better see change.

|        |
|--------|
| (b)(4) |
| (b)(4) |

Not news, but with this format one gets a sense of the magnitude.

I would love to hear your thoughts on this new data view fully recognizing you many pressing issues you are admirably juggling.

As always, I'd be happy to pull together our data gurus to discuss this data or their approaches to measurement and tracking beyond this (influenza comes to mind), and implications, application to COVID vaccine tracking.

I welcome any thoughts, questions, or comments on what is or isn't here –  
Julian

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

**From:** Leonard Friedland  
**Sent:** Fri, 2 Oct 2020 13:19:12 +0000  
**To:** Dooling, Kathleen L. (CDC/DDID/NCIRD/DVD); Oliver, Sara Elizabeth (CDC/DDID/NCIRD/DVD); Cohn, Amanda (CDC/DDID/NCIRD/OD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD); Messonnier, Nancy (CDC/DDID/NCIRD/OD)  
**Cc:** Barbara Howe  
**Subject:** Question from GSK Vaccines

Dear Kathleen, Sara, Amanda, Jessica and Nancy,

Thank you for the work you are leading in in anticipation of future availability of COVID-19 vaccines.

Recognizing the initial clinical trials being conducted to support to FDA authorization/approval of the COVID-19 vaccines do not include coadministration data with CDC recommended adult vaccines, we are interested to gain insights into CDC thinking on the subject of when an adult goes to pharmacy or doctor office to get a COVID-19 vaccine and they are also due for a flu, Tdap, pneumococcal or shingles vaccine; or vice versa the patient is going to get an adult recommended vaccine and they could also receive a COVID-19 vaccine.

Does ACIP: 1) recommend to not miss the opportunity and receive COVID-19 vaccine and the other adult recommended vaccine; 2) it is not recommended to receive other recommended vaccines until after completing the COVID-19 vaccine series, or 3) use shared clinical decision making about administering other recommended vaccines until after completing the COVID-19 vaccine series.

Thank you  
Best regards, Len

Leonard Friedland, MD  
VP, Scientific Affairs and Public Health  
GSK Vaccines

(b)(6)

**GSK monitors email communications sent to and from GSK in order to protect GSK, our employees, customers, suppliers and business partners, from cyber threats and loss of GSK Information. GSK monitoring is conducted with appropriate confidentiality controls and in accordance with local laws and after appropriate consultation.**

**From:** Ritchey, Julian /US  
**Sent:** Tue, 6 Oct 2020 23:03:27 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD);Wharton, Melinda (CDC/DDID/NCIRD/ISD);Santoli, Jeanne (CDC/DDID/NCIRD/ISD)  
**Subject:** COVID Impact Data - Week of 9/12 Update  
**Attachments:** State Claims\_External Parties 10022002.pptx, IQVIA Claims Variance Tracker 10022020.xlsx

Dear Nancy, Melinda, and Jeanne --  
Updated data.

I believe I shared last time the summary spreadsheet the team developed to make the trends from the graphic data a little easier to see.

Simple read (b)(4)

(b)(4)

Please let me know any interest in further discussion.  
Hope you all are staying well amid the many challenges you are facing.

Julian



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

**From:** Cane, Alejandro  
**Sent:** Mon, 12 Oct 2020 21:43:47 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD); Wharton, Melinda (CDC/DDID/NCIRD/ISD)  
**Subject:** Contact from Pfizer

Dear Nancy and Melinda

I hope all is going well.

Thank you again for all of the work you and your team on doing, not only to address COVID-19, but also to manage all other vaccine matters before CDC at this extraordinary time.

I'm writing to ask for an hour-long meeting with you to discuss two issues. (b)(4)

(b)(4)

On our team, my colleagues, David Hering (head of North America Vaccines), Erin Byrczek (VP of U.S. Pediatric & Adolescent Vaccines), Drew Gess (our CDC director), and Lisa Coen (head of US Public Affairs) would likely join the meeting.

I know you are incredible busy; I really appreciate your time reading this email.

Thank you for your consideration of our request.

Best regards,

Ale

Alejandro Cané, MD PhD  
North America Vaccines Medical and Scientific Affairs Lead  
Pfizer Biopharmaceuticals Group  
Complejo Thames Office Park  
Colectora Panamericana 1804, 1 Piso Sector "B" Lado Sur  
Villa Adelina (CP 1607EEV) Pcia Buenos Aires-Argentina  
Tel: (b)(6)  
Mobile: (b)(6)  
e mail: (b)(6)





Pfizer



Pfizer  
Biopharmaceuticals  
Group

**From:** Ritchey, Julian /US  
**Sent:** Thu, 15 Oct 2020 20:41:51 +0000  
**To:** Messonnier, Nancy (CDC/DDID/NCIRD/OD);Wharton, Melinda (CDC/DDID/NCIRD/ISD);Santoli, Jeanne (CDC/DDID/NCIRD/ISD)  
**Subject:** Updated post-COVID Claims Data  
**Attachments:** State Claims\_External Parties 10142020 - Read-Only.pptx

Dears –

Attached please find the most recent pulled of the claims data.

(b)(4)

I welcome your thoughts and questions –  
Julian

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

**From:** Cane, Alejandro  
**Sent:** Mon, 19 Oct 2020 18:57:39 +0000  
**To:** Cohn, Amanda (CDC/DDID/NCIRD/OD); Messonnier, Nancy (CDC/DDID/NCIRD/OD); Wharton, Melinda (CDC/DDID/NCIRD/ISD); Painter, Elizabeth (CDC/DDID/NCIRD/ID); Hering, David; Coen, Lisa; Gess, Andrew J; Byrczek, Erin M  
**Subject:** RE: PFIZER Vaccines update

Thanks for letting us know Amanda

Talk you soon

Best regards,

Ale

**From:** Cohn, Amanda (CDC/DDID/NCIRD/OD) <anc0@cdc.gov>  
**Sent:** Monday, October 19, 2020 3:56 PM  
**To:** Cane, Alejandro <(b)(6)> Messonnier, Nancy (CDC/DDID/NCIRD/OD) <nar5@cdc.gov>; Wharton, Melinda (CDC/DDID/NCIRD/ISD) <mew2@cdc.gov>; Painter, Elizabeth (CDC/DDID/NCIRD/ID) <ocv3@cdc.gov>; Hering, David <(b)(6)>; Coen, Lisa <(b)(6)>; Gess, Andrew J <(b)(6)>; Byrczek, Erin M <(b)(6)>  
**Subject:** [EXTERNAL] RE: PFIZER Vaccines update

Hi all,

Apologies in advance, but we are going to have to shift this to a 30 minute meeting, we were just asked to be on an urgent call at 3:30. We can find another half hour if we need to finish the discussion. Talk to you in a few,

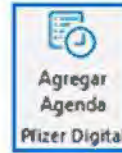
Amanda

-----Original Appointment-----

**From:** Cane, Alejandro <(b)(6)>  
**Sent:** Tuesday, October 13, 2020 11:23 AM  
**To:** Cane, Alejandro; Messonnier, Nancy (CDC/DDID/NCIRD/OD); Wharton, Melinda (CDC/DDID/NCIRD/ISD); Cohn, Amanda (CDC/DDID/NCIRD/OD); Painter, Elizabeth (CDC/DDID/NCIRD/ID); Hering, David; Coen, Lisa; Gess, Andrew J; Byrczek, Erin M  
**Subject:** PFIZER Vaccines update  
**When:** Monday, October 19, 2020 4:00 PM-5:00 PM (UTC-03:00) City of Buenos Aires.  
**Where:**

Las reuniones son más efectivas con agendas bien definidas.  
*¡El nuevo Asistente de agenda digital de Pfizer te puede ayudar!*

Para comenzar, haz clic en "Agregar agenda" en la barra de arriba.



-- Do not delete or change any of the following text. --

## 1. [Click to Join the Meeting](#)

**IMPORTANT NOTICE: Please note that this Webex service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. By joining this session, you automatically consent to such recordings. If you do not consent to being recorded, discuss your concerns with the host or do not join the session.**

## 2. Join the Audio

- From a Pfizer office - select Call Me (and have it call your office or conference phone)
  - Not working in a Pfizer office or using a mobile phone?
    - From a **computer** with a good Internet connection, select **Call Using Computer+**
    - From a **mobile device** with Wi-Fi access, select **Call Over Internet+**
    - If no Internet or data connection is available, see below for dial-in details
- + Use a headset or mobile phone earbuds for the best quality sound**

### WebEx Meeting and Support Details

Meeting number (b)(6) Meeting password (b)(6)

### No Internet or data connection?

If you are located in a different country than the one shown, find your country's dial-in number using the **Global call-in numbers** link below - please use the **TOLL number**, if available:

### Join by phone

(b)(6) Call-in toll number (US/Canada)

Access code: (b)(6)

[Global call-in numbers](#) | [Toll-free calling restrictions](#)