DEPARTMENT OF HEALTH & HUMAN SERVICES

Health Resources and Services Administration

Rockville, MD 20857

March 26, 2020

Sent via Email
Allison Lucas, Esq.
Siri & Glimstad LLP
200 Park Avenue, 17th Floor
New York, NY 10166
foia@sirillp.com

Re: Health Resources and Services Administration (HRSA) Freedom of Information Act (FOIA) Request Case Number 20F076

Dear Ms. Lucas:

This is the final response to your FOIA request dated December 31, 2019. In summary, you requested email communications from January 1, 2017, to January 3, 2020, that were sent to or from Narayan Nair, a former HRSA employee, as well as those in which he was copied in the CC or BCC lines. The emails you specifically requested are those containing one or more of the following terms: Stanley Plotkin (and various iterations of his email addresses); Advisory Committee on Immunization Practices; vaccine hesitancy; antivaccine; antivaccination; anti-vaxx; anti-vax; antivax; and antivaxx.

Upon receipt, your request was sent to HRSA's Office of Information Technology (OIT) and the National Vaccine Injury Compensation Program (VICP) in the Healthcare Systems Bureau for a search. OIT informed our office that Narayan Nair left HRSA in June 2019 and his accounts were deleted 45 days after his departure, pursuant to the email retention policy. However, VICP located 159 pages of responsive records. Of those, 134 pages are being released in their entirety. I have determined to withhold portions of 25 pages under FOIA Exemptions 3, 5, and 6, 5 U.S.C. § 552(b)(3), (b)(5), and (b)(6).

Exemption 3 allows for the withholding of information prohibited from disclosure by another statute. The statute which applies in this instance is 42 U.S.C. § 300aa-12(d)(4)(A). It states that vaccine compensation petitions may not be disclosed to a person who is not a party to the proceeding without the express written consent of the person who submitted the information.

Exemption 5 protects privileged communications within or between agencies, including those protected by the following privileges: deliberative process privilege, which is to prevent injury to the quality of agency decisions; attorney-client privilege, which are confidential communications between an attorney and his/her client relating to a legal matter; and attorney work-product privilege, which protects documents and other memoranda prepared by an attorney in contemplation of litigation.

Exemption 6 protects information about individuals in "personnel and medical files and similar files" when the disclosure of such information would constitute a clearly unwarranted invasion of privacy. The

withheld information in this instance includes medical records, patient information, and personal telephone numbers.

The U.S. Department of Health and Human Services (HHS) policy calls for the fullest responsible disclosure consistent with the requirements of administrative necessity and confidentiality as recognized by the FOIA, 5 U.S.C. § 552 and HHS' FOIA's regulations at 45 CFR Part 5.

If you believe that the information withheld should not be exempt from disclosure or that this response constitutes an adverse determination, you may appeal. By filing an appeal, you preserve your rights under FOIA and give the agency a chance to review and reconsider your request and the agency's decision.

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

Kim Hutchinson
Deputy Agency Chief FOIA Officer
U.S. Department of Health and Human Services
Office of the Assistant Secretary for Public Affairs
Room 729H
200 Independence Avenue, SW
Washington, DC 20201

Please clearly mark both the envelope and your letter "HRSA Freedom of Information Act Appeal."

If you would like to discuss our response before filing an appeal to attempt to resolve your dispute without going through the appeals process, you may contact HRSA's FOIA Public Liaison for assistance at:

Denise F. Wallace
HRSA FOIA Public Liaison
U.S. Department of Health and Human Services
Health Resources and Services Administration
Freedom of Information Act Office
5600 Fishers Lane, 13N114
Rockville, MD 20857
Telephone: 301-443-2865
Email: foia@hrsa.gov

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

Office of Government Information Services
National Archives and Records Administration
8601 Adelphi Road–OGIS
College Park, MD 20740-6001
Telephone: 202-741-5770

Fax: 202-741-5769
Toll-Free: 1-877-684-6448
Email: ogis@nara.gov

There will be no charges in this instance because the billable costs are less than our threshold of $25.

If you have any questions, please do not hesitate to contact my office at 301-443-2865 or FOIA@hrsa.gov.

Sincerely,

D.F. Wallace

For Thomas Flavin
Freedom of Information Officer

Enclosure

From: Stanley Plotkin
To: "Narayan Nair"; Rubin, Mary (HRSA); "Meissner, Cody"
Subject: RE: VICP: Reactions analysis
Date: Friday, December 06, 2019 3:16:23 PM

Dear All:

I have bad news or good news depending on how you look at it. The paper we were going to write on the numerical relationship between compensation and vaccination has already been written and submitted for publication. I can say no more as I am reviewing the paper.

Stan

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Tuesday, September 03, 2019 8:18 AM
To: 'Narayan Nair'; 'Rubin, Mary (HRSA)'
Cc: 'Meissner, Cody'
Subject: RE: VICP: Reactions analysis

Excellent.
S

From: Narayan Nair [mailto: (b) (6)
Sent: Monday, September 02, 2019 10:02 PM
To: Rubin, Mary (HRSA)
Cc: Stanley Plotkin; Meissner, Cody
Subject: Re: VICP: Reactions analysis

Hello, I can get the vaccine doses distributed numbers.

Sent from my iPhone

On Sep 2, 2019, at 4:48 PM, Rubin, Mary (HRSA) <MRubin@hrsa.gov> wrote:

> Hi Stanley,
>
> Regarding anaphylaxis, these are all the concessions we have. The search was for all vaccines.
>
> Regarding encephalopathy related to MMR, what details do we need?
>
> I'll be at the NVAC meeting on Sept 17-18, so won't be available then. I'm available on Thurs Sept 19 (9 – 2:30p) and Friday Sept 20 (9-10, 1-4p).
>
> Mary
>
> ---
>
> **From:** Stanley Plotkin <stanley.plotkin@vaxconsult.com>
> **Sent:** Monday, September 02, 2019 4:28 PM
> **To:** Rubin, Mary (HRSA) <MRubin@hrsa.gov>; 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>; 'Narayan Nair' < (b) (6)>

Subject: RE: VICP: Reactions analysis

Dear Mary:

Thank you for this. My comments are

Anaphylaxis is rare. Are there other cases? Perhaps for this reaction we should compile all, regardless of vaccine.

Intussusception works out to about [redacted] per year. Not bad.

GBS is about [redacted] per year. We should try to get a number for GBS unrelated to vaccines.

Can we get more detail about encephalopathy related to MMR?

Now we need figures for vaccine doses administered. Who will do that?

I will be on a work trip to Europe starting Wednesday. Can we schedule a call on September 17? I could also do it tomorrow morning but that is short notice.

Stanley

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Monday, September 02, 2019 4:04 PM
To: Stanley Plotkin; Meissner, Cody; Narayan Nair
Subject: VICP: Reactions analysis

Hi Stanley, and Cody,

Here are the concessions divided into the vaccines. I realize we are only focusing on Pertussis, MMR, Rotavirus and Influenza but the list below includes the numbers for Td, just so we know how all the concessions were distributed.

Pls. let me know if there are any questions or if you'd like to set up a call.

Thanks!

Mary

Td	Anaphylaxis Brachial neuritis **Total**	[redacted]
Tdap/DTaP	Anaphylaxis Brachial neuritis Encephalopathy **Total**	[redacted]
MMR	Anaphylaxis Encephalopathy ITP **Total**	[redacted]
Rotavirus	Intussusception	[redacted]

Influenza	GBS	(b) (6), (b)
Total concessions		187

Mary Nythel Rubin, MD
Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
Department of Health and Human Services
mrubin@hrsa.gov
(301)443-4047

From: Stanley Plotkin
To: "Meissner, Cody"; Rubin, Mary (HRSA); "Narayan Nair"
Subject: RE: [EXT] article
Date: Thursday, November 14, 2019 12:50:31 PM

OK. For information, later dates on which I could attend are November 27 or any day the following week except Dec 3.
Stanley

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Thursday, November 14, 2019 12:33 PM
To: Stanley Plotkin; 'Rubin, Mary (HRSA)'; 'Narayan Nair'
Subject: RE: [EXT] article

I will not be able to circulate a draft before Nov 21, the date of our proposed call so we should postpone that call.
I hope to have a draft soon
Cody

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Monday, September 30, 2019 3:03 PM
To: Meissner, Cody; 'Rubin, Mary (HRSA)'; 'Narayan Nair'
Subject: [EXT] article

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

I forgot to draw your attention to an article by Arya et al from the FDA in Vaccine 2019.37:6543 that reports on GBS after influenza vaccine of about 1 per million doses, but there was variation between vaccines, with high dose giving a higher signal.
Stanley

From: Narayan Nair
To: Rubin, Mary (HRSA)
Subject: Re: Geoff Evans
Date: Thursday, October 24, 2019 3:58:00 PM

Ok thanks. Glad to hear ACIP went well.

Sent from my iPhone

On Oct 24, 2019, at 2:59 PM, Rubin, Mary (HRSA) <MRubin@hrsa.gov> wrote:

> He uses this one too: Geoffrey Evans <s (b) (6)>
>
> ---
>
> **From:** Rubin, Mary (HRSA)
> **Sent:** Thursday, October 24, 2019 2:50 PM
> **To:** Narayan NAIR (b) (6)
> **Subject:** RE: Geoff Evans
>
> Hi Narayan,
>
> Things are good. I'm at the airport waiting for my flight home from ACIP meeting. Folks asked how you were doing – John Begney (?) (NIH), Dorian Fink and Eric Duessing. Eric (DOD) (b) (6). Anyway, they say hi.
>
> Here's Geoff's email: (b) (6)
>
> Mary
>
> ---
>
> **From:** Narayan NAIR < (b) (6)
> **Sent:** Thursday, October 24, 2019 1:40 PM
> **To:** Rubin, Mary (HRSA) <MRubin@hrsa.gov>
> **Subject:** Geoff Evans
>
> Hello Mary,
> Hope you are OK. Do you happen to have Geoff Evans email? I wanted to ask him a question.
>
> Narayan

From:	Stanley Plotkin
To:	Rubin, Mary (HRSA); "Meissner, Cody"; "Narayan Nair"
Subject:	RE: [EXT] RE: VICP: Reactions analysis
Date:	Tuesday, September 03, 2019 4:14:40 PM

Yes
Stanley

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Tuesday, September 03, 2019 3:55 PM
To: Meissner, Cody; 'Stanley Plotkin'; 'Narayan Nair'
Subject: RE: [EXT] RE: VICP: Reactions analysis

Sept 30 works for me too. Does 1 or 2 pm start on Sept 30 work for everyone?

From: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Sent: Tuesday, September 03, 2019 3:29 PM
To: 'Stanley Plotkin' <stanley.plotkin@vaxconsult.com>; 'Narayan Nair' <(b) (6)>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: [EXT] RE: VICP: Reactions analysis

September 30 afternoon is okay for me.
VIS is on agenda for ACCV and I will let you know.
Cody

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Tuesday, September 03, 2019 2:53 PM
To: Meissner, Cody; 'Narayan Nair'; 'Rubin, Mary (HRSA)'
Subject: RE: [EXT] RE: VICP: Reactions analysis

Unfortunately I will be at a meeting on Spetember 26 and 27. That leaves September 30.
Cody, on another subject perhaps you could inquire at the COID why it would not follow my suggestions about lodging complaint to the FDA about package inserts. I understand that someone at AAP was against it, but COID seems to have rolled over. Also, CDC is supposed to be revising the Vaccine Information Statements,, a process that COID should be involved in, but is not as far as I know.
Stanley

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Tuesday, September 03, 2019 1:52 PM
To: 'Stanley Plotkin'; 'Narayan Nair'; 'Rubin, Mary (HRSA)'
Subject: RE: [EXT] RE: VICP: Reactions analysis

I will be at NVAC and hopefully Mary and I can find a few minutes to talk.
I will be at COID meeting in Chicago on September 23-25 so not able to participate in call.

September 26 or 27 in afternoon works for conference call if that is okay with others.
Cody

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Tuesday, September 03, 2019 8:18 AM
To: 'Narayan Nair'; 'Rubin, Mary (HRSA)'
Cc: Meissner, Cody
Subject: [EXT] RE: VICP: Reactions analysis

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

Excellent.
S

From: Narayan Nair [(b) (6)
Sent: Monday, September 02, 2019 10:02 PM
To: Rubin, Mary (HRSA)
Cc: Stanley Plotkin; Meissner, Cody
Subject: Re: VICP: Reactions analysis

Hello, I can get the vaccine doses distributed numbers.

Sent from my iPhone

On Sep 2, 2019, at 4:48 PM, Rubin, Mary (HRSA) <MRubin@hrsa.gov> wrote:

> Hi Stanley,
>
> Regarding anaphylaxis, these are all the concessions we have. The search was for all vaccines.
>
> Regarding encephalopathy related to MMR, what details do we need?
>
> I'll be at the NVAC meeting on Sept 17-18, so won't be available then. I'm available on Thurs Sept 19 (9 – 2:30p) and Friday Sept 20 (9-10, 1-4p).
>
> Mary
>
> ---
>
> **From:** Stanley Plotkin <stanley.plotkin@vaxconsult.com>
> **Sent:** Monday, September 02, 2019 4:28 PM
> **To:** Rubin, Mary (HRSA) <MRubin@hrsa.gov>; 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>; 'Narayan Nair' <Nnair1968@comcast.net>
> **Subject:** RE: VICP: Reactions analysis
>
> Dear Mary:

Thank you for this. My comments are
Anaphylaxis is rare. Are there other cases? Perhaps for this reaction we should compile all, regardless of vaccine.
Intussusception works out to about [redacted] per year. Not bad.
GBS is about [redacted] per year. We should try to get a number for GBS unrelated to vaccines.
Can we get more detail about encephalopathy related to MMR?
Now we need figures for vaccine doses administered. Who will do that?
I will be on a work trip to Europe starting Wednesday. Can we schedule a call on September 17? I could also do it tomorrow morning but that is short notice.
Stanley

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Monday, September 02, 2019 4:04 PM
To: Stanley Plotkin; Meissner, Cody; Narayan Nair
Subject: VICP: Reactions analysis

Hi Stanley, and Cody,
Here are the concessions divided into the vaccines. I realize we are only focusing on Pertussis, MMR, Rotavirus and Influenza but the list below includes the numbers for Td, just so we know how all the concessions were distributed.

Pls. let me know if there are any questions or if you'd like to set up a call.

Thanks!

Mary

Td	Anaphylaxis	[redacted]
	Brachial neuritis	
	Total	
Tdap/DTaP	Anaphylaxis	[redacted]
	Brachial neuritis	
	Encephalopathy	
	Total	
MMR	Anaphylaxis	
	Encephalopathy	
	ITP	
	Total	
Rotavirus	Intussusception	
Influenza	GBS	

Total concessions	187

Mary Nythel Rubin, MD
Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
Department of Health and Human Services
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(301)443-4047

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Please consider the environment and the security of the information contained within or attached to this e-mail before printing or saving to an insecure location.

From:	Stanley Plotkin
To:	Rubin, Mary (HRSA)
Subject:	RE: [EXT] RE: reactions analysis
Date:	Monday, August 12, 2019 9:58:54 AM

No, an emergency has arisen and I will not be available at that time. I could do it at 9am on Friday or nearly any time on Thursday, but on Friday I will be in the air.
Stanley

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Monday, August 12, 2019 9:52 AM
To: Stanley Plotkin; 'Meissner, Cody'
Cc: 'Narayan Nair'
Subject: RE: [EXT] RE: reactions analysis

Good morning,

Following up on our planned phone call – does Friday 2:30 pm work?

Thanks!
Mary

From: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Sent: Friday, August 09, 2019 1:52 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>; 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>
Cc: 'Narayan Nair' <(b) (6)>
Subject: RE: [EXT] RE: reactions analysis

I could make that also, but let's pin it down asap.
Stanley

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Friday, August 09, 2019 1:27 PM
To: Meissner, Cody; 'Stanley Plotkin'
Cc: Narayan Nair
Subject: RE: [EXT] RE: reactions analysis

Hi Stanley and Cody,

Can we arrange for a 2:30 or 3pm call on Friday, instead?

Cody – yes, brachial neuritis is a separate entity from SIRVA. It was put on the Table in 1997. When Narayan and I were confirming brachial neuritis cases, some of the cases on the list ended up being SIRVA concessions and those are not included in the numbers.

Mary

From: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Sent: Friday, August 09, 2019 1:17 PM
To: 'Stanley Plotkin' <stanley.plotkin@vaxconsult.com>
Cc: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: [EXT] RE: reactions analysis

Dear Stanley,
Can your assistant set up the phone call or should I do it?
Cody

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Friday, August 09, 2019 12:52 PM
To: Meissner, Cody
Subject: RE: [EXT] RE: reactions analysis

I confirm that 1:320 pm on August 16 is OK for me.
Stanley

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Friday, August 09, 2019 12:24 PM
To: 'Stanley Plotkin'; 'Rubin, Mary (HRSA)'; 'Narayan Nair'
Subject: RE: [EXT] RE: reactions analysis

Dear Mary,
Friday August 16 at 1:30 pm Boston time or after works best for me.
Assume brachial neuritis is a different classification than SIRVA?
Thinking about American Association of Orthopedic Surgeons position that SIRVA is not a real diagnosis.
Cody

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Friday, August 09, 2019 8:52 AM
To: 'Rubin, Mary (HRSA)'; 'Narayan Nair'
Cc: Meissner, Cody
Subject: [EXT] RE: reactions analysis

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

Dear Mary:
Excellent! I am available any day next week except Wednesday but the best times would be Monday all day

Tuesday all day
Thursday after 11am
Friday except 11:30 to 1:30
Stanley

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Friday, August 09, 2019 8:29 AM
To: Stanley Plotkin; Narayan Nair
Cc: Meissner, Cody
Subject: RE: reactions analysis

Hi Stanley and Cody,

Here are our confirmed numbers (concessions with vaccine administration date between 1/1/2006 and 12/31/2017):

Anaphylaxis = 4
Brachial Neuritis =11
Encephalopathy =18
ITP = 12
Intussusception = 23
GBS = 99

Let me know when you are available for a call.

Thanks!

Mary

Mary Nythel Rubin, MD
Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
Department of Health and Human Services
mrubin@hrsa.gov
(301)443-4047

From: Stanley Plotkin <Stanley.plotkin@vaxconsult.com>
Sent: Thursday, July 11, 2019 5:44 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Cc: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: Re: reactions analysis

I think it would be best to have the call after you've completed the numbers and I will be glad to

arrange
Stanley

Sent from my iPhone

On Jul 11, 2019, at 4:53 PM, Nair, Narayan (HRSA) <NNair@hrsa.gov> wrote:

> Hello, sorry for the delay in responding. Mary and I are confirming the final numbers at this stage and I think we should be complete with that soon. I am happy to participate in a conference call
>
> Narayan Nair, MD
> CAPT, USPHS
> Division Director
> Division of Injury Compensation Programs
> Healthcare Systems Bureau
> Health Resources and Services Administration
> 5600 Fishers Lane, Room 8N23
> Rockville, MD 20857
>
> <image001.png>
> <image012.jpg> <image013.jpg> <image014.jpg> <image015.jpg>
> <image016.jpg>
>
> ---
>
> **From:** Stanley Plotkin <stanley.plotkin@vaxconsult.com>
> **Sent:** Monday, July 08, 2019 9:17 AM
> **To:** 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
> **Subject:** reactions analysis
>
> Dear Cody and Narayan:
> Where are we with this? Should we have a conference call with Helen to plan the way forward? Who will start writing? We need an outline. Also, I am conscious that Narayan (b) (6) so communication with him needs adjustment.
> Stanley

The information in this e-mail is intended only for the person to whom it is addressed. If you

believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Tufts Medical Center HIPAA Hotline at (617) 636-4422. If the e-mail was sent to you in error but does not contain patient information, contact the sender and properly dispose of the e-mail.

Please consider the environment and the security of the information contained within or attached to this e-mail before printing or saving to an insecure location.

From: Stanley Plotkin
To: "Meissner, Cody"; Nair, Narayan (HRSA); Rubin, Mary (HRSA)
Subject: RE: Published Rates of AE
Date: Wednesday, June 12, 2019 12:22:00 PM

Dear Cody:
This is very helpful to enable us to select background rates. I will read carefully. Of course, we will have to make some judgments as to the validity and relevance of each source.
Stanley

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Wednesday, June 12, 2019 11:59 AM
To: 'Stanley Plotkin'; 'Nair, Narayan (HRSA)'; 'Rubin, Mary (HRSA)'
Subject: Published Rates of AE

Dear Stanley, Narayan, Mary
Attached is an updated list of published papers that indicate rates of AEs after vaccination.
The idea is to use these reference rates to compare with award rates from VICP.
Cody

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Tuesday, May 07, 2019 11:46 AM
To: 'Nair, Narayan (HRSA)'; Meissner, Cody
Subject: [EXT] RE: call on Friday

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

I thought I would add this attachment. I no longer remember who sent it, but it is germane.
Stanley

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Tuesday, May 07, 2019 9:35 AM
To: 'Nair, Narayan (HRSA)'; 'Meissner, Cody'
Subject: call on Friday

Dear Narayan and Cody:

I thought I would summarize what we are trying to do for Friday's call.

The objective is to determine the rate of awards by the compensation system for reactions to specific vaccines. In his email of April 30, Narayan identified the time covered as calendar years 2006-2017, thus 12 years, although at one point it was said we might have to stop at 2016. The reactions identified in that email were anaphylaxis, brachial neuritis, encephalopathy, ITP, intussusceptions, arthritis and Guillain-Barré Syndrome. However, in a prior email on March 28 different figures were given from 2000, so that has to be straightened out.

The reactions awarded by the table are

1. Vaccines containing cellular pertussis antigens or tetanus toxoids
    a. Anaphylaxis
    b. Shoulder injury related to vaccine administration
2. Vaccines containing MMRV
    a. Encephalopathy or encephalitis (vaccine associated acute disseminated encephalomyelitis)
    b. Chronic arthritis
    c. Thrombocytopenic purpura
3. Rotavirus vaccines
    a. Intussusception
4. Influenza vaccines
    a. Guillain-Barre syndrome (also MMR, HPV, meningococcal vaccines)

But I think we are excluding shoulder injury because it is physician caused, not vaccine caused.

So the data on vaccine doses given relate to DTaP or T, MMR (not sure about V), rotavirus, and influenza. Not clear to me whether other vaccines must be taken into account for GBS.

So on our call let's focus on just exactly what data we need and how to get them.

Looking forward to Friday,
Stanley

From:	Stanley Plotkin
To:	Nair, Narayan (HRSA); "Meissner, Cody"
Cc:	Rubin, Mary (HRSA)
Subject:	RE: [EXT] RE: AE events reported to Vaccine Injury Program
Date:	Wednesday, May 01, 2019 1:34:13 PM
Attachments:	image001.png

OK. Unless I hear otherwise I will set up for 9:30 am on May 10
S

From: Nair, Narayan (HRSA) [mailto:NNair@hrsa.gov]
Sent: Wednesday, May 01, 2019 1:31 PM
To: Meissner, Cody; 'Stanley Plotkin'
Cc: Rubin, Mary (HRSA)
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

I am on travel May 3 but May 10 am works.

Narayan Nair, MD
CAPT, USPHS
Division Director
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
5600 Fishers Lane, Room 8N23
Rockville, MD 20857

From: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Sent: Wednesday, May 01, 2019 12:34 PM
To: 'Stanley Plotkin' <stanley.plotkin@vaxconsult.com>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
Cc: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

May 3 or May 10 in AM is okay for me.
Cody

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Wednesday, May 01, 2019 9:40 AM
To: 'Nair, Narayan (HRSA)'; Meissner, Cody
Cc: 'Rubin, Mary (HRSA)'

Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Dear Narayan and Cody:

These data are beginning to look golden. To move things forward I think we need another conference call. I could do that this Friday morning and anytime May 7, 8, or 10. Please tell me when you are available.

Stanley

From: Nair, Narayan (HRSA) [mailto:NNair@hrsa.gov]
Sent: Tuesday, April 30, 2019 2:11 PM
To: Stanley Plotkin; Meissner, Cody
Cc: Rubin, Mary (HRSA)
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Good afternoon Stanley and Cody,
I have updated our search. We realized there was an error in the previous data but here is what I believe is more accurate information.

Population studied:

- All cases adjudicated between January 1, 2006 and December 31, 2017. This time frame was chosen to align with the vaccine doses distributed data that is available

Inclusion Criteria:

- Of the adjudicated cases, I included cases that were reviewed and conceded by HHS as meeting the criteria of Vaccine Injury Table for the specified injury.

Exclusion Criteria:

- Cases that were not adjudicated in the above time frame
- Cases that were compensated but not conceded by HHS as meeting the criteria as a Table Injury. An example of this may be a case of where an individual alleged Guillain Barre Syndrome where the onset of symptoms occurred more than 42 days after vaccination. This is not a case we would concede but nonetheless we may opt to provide compensate the claim under a litigative risk settlement for a variety of reasons.
- Cases where the individual did not have effects of the injury last greater than 6 months, or the injury did not result resulted in inpatient hospitalization AND surgical intervention or death. To be eligible for compensation all petitioners must meet this criteria

Limitations:

- Individuals who suffered a vaccine injury but symptoms resolved prior to 6 months would not be captured in this data because of the severity requirement outlined above
- Our database was designed to store and retrieve medical records and process hundreds of millions of dollars of payments in a timely/efficient manner. It does all of these very well but it is less effective as a research tool and was never designed for that. Because of this there could be errors in how an injury was recorded. I have tried to verify all the information but have not completed that process yet.
- We have cumulative data on the number of doses of vaccine distributed between

2006-2017 but some of the injuries were not on the table for that entire time span. This may make it difficult to project incidence. I think this will mainly be an issue for GBS but I am not sure.

- There of course will be a population of people who met our criteria for a Table Injury but were not aware of the VICP and did not file with the program. By law everyone is to receive a Vaccine Information Statement when they receive the vaccine and this provides info on the VICP so hopefully this is not a large number.

Anaphylactic shock [redacted] cases associated with Td vaccine
Brachial Neuritis – [redacted] cases associated with Tdap vaccine
Encephalopathy/encephalitis- [redacted] cases associated with DTaP-IPV-HIB vaccine
ITP – [redacted] cases associated with MMR-V vaccine
Intussusception [redacted] cases associated with Rotavirus vaccine
Arthritis – [redacted] in this time frame
GBS – [redacted] cases associated with influenza vaccine

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CAPT, USPHS
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Healthcare Systems Bureau
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Rockville, MD 20857

HRSA

From: Stanley Plotkin <Stanley.plotkin@vaxconsult.com>
Sent: Thursday, March 28, 2019 5:16 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Cc: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Subject: Re: [EXT] RE: AE events reported to Vaccine Injury Program

Excellent progress! We will need attribution of each reaction to which vaccines
Stan

Sent from my iPhone

On Mar 28, 2019, at 2:59 PM, Nair, Narayan (HRSA) <NNair@hrsa.gov> wrote:

Here is the revised data: From 2000 to present here are the number of cases HHS has conceded that the vaccine caused met the table definition of the condition listed and presumed to have caused the injury.
Anaphylactic shock –6 cases
Brachial Neuritis 25 cases
Encephalopathy/encephalitis- 38
ITP – 14
Intussusception -4
Arthritis -5
GBS – 69

I believe this is more accurate than what I previously shared. I am working on getting numbers of vaccine distributed for these years and will let you know as soon as I have them.

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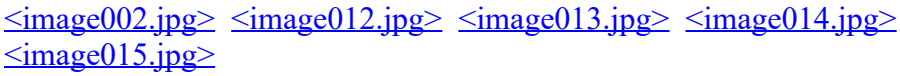

From: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Sent: Saturday, March 23, 2019 1:32 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Interesting VRBPAC meeting yesterday. Decision was to use A/Kansas/14/2017 in next season's influenza vaccine. The majority of A/H3N2 viruses isolated this year were subclade 3C.2a1b but in recent months the predominant clade has been 3C.3a, with little antibody cross reactivity. This clade seems to be more biologically fit than 3C.2a1b and seems to be replacing the most common strain. The A/Kansas strain is 3C.3a and is projected by WHO to be a greater concern next season in Northern Hemisphere so that will be in the vaccine. There was a 16 day delay on deciding on which A/H3N2 strain would be distributed to pharmaceutical companies and some concern that if strains do not grow well, there might be a delay in vaccine availability.

Narayan, your data are interesting. Interesting that reported encephalopathy/encephalitis cases are about 6 times that of GBS. To address Stanley's question, overall encephalitis is more common <1 year of age (13/100,000) and >65 years (10/100,000). In between ages, rates are 4-8/100,000. In, 1/3 to 2/3 of encephalitis cases, the etiology is undetermined after workup. (References: CID 2003;36:731, CID 2002;35:175, CID 2006;66:75). I am working to get rates of encephalopathy. Rates of the two are not always clearly reported separately.

DTaP was approved by FDA in 1991 and recommended in place of DTwP for doses 4 and 5. In 1997, ACIP recommended DTaP be used for all 5 doses in childhood schedule. So there will be a transition period between 1991 and 1997 when children received a variable number of the two vaccines. Infanrix approved in 1997 and Daptacel approved in 2002.

Cody

From: Nair, Narayan (HRSA) [NNair@hrsa.gov]
Sent: Friday, March 22, 2019 12:49 PM
To: Stanley Plotkin; Meissner, Cody
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Ok will do.

Narayan Nair, MD
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5600 Fishers Lane, Room 8N23
Rockville, MD 20857

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From: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Sent: Friday, March 22, 2019 12:44 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

I don't remember off hand, but the trials were done in the 1990s and since you said that the data after 2000 were more accurate, I suggest 2001 onwards.

Stanley

From: Nair, Narayan (HRSA) [mailto:NNair@hrsa.gov]
Sent: Friday, March 22, 2019 12:40 PM
To: Stanley Plotkin; 'Meissner, Cody'
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

This sounds like a good approach. What year was the acellular pertussis was used instead of whole cell? I can run the numbers starting in that year.

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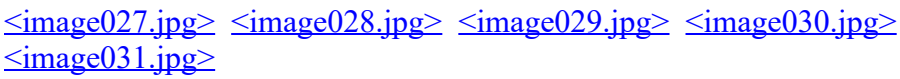

From: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Sent: Friday, March 22, 2019 10:28 AM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Dear Narayan:

This is a terrific start and looks promising. However, I have one caution: we want data that are applicable today. I hadn't thought about the switch from whole cell to acellular but I think it is important that we focus on the present, so I would suggest that we use only data from the introduction of acellular onwards. That would enable the use of data from 2000s on, which you say are more accurate. That should also simplify the determination of the number of doses, which should be vaccine-specific. The latter is particularly important with regard to encephalopathy. In that regard I wonder if Cody has any ideas about how to determine the background incidence of encephalopathy?

Stanley

From: Nair, Narayan (HRSA) [mailto:NNair@hrsa.gov]
Sent: Friday, March 22, 2019 9:49 AM
To: Stanley Plotkin; 'Meissner, Cody'
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

I have some preliminary data to share: From 1988 to present here are the number of cases HHS has conceded that the vaccine caused met the table definition of the condition listed and presumed to have caused the injury.
Anaphylactic shock –22 cases
Brachial Neuritis 29 cases
Encephalopathy/encephalitis- 405
ITP – 16
Intussusception -4
Arthritis -12
GBS – 70

I had a few comments/points of clarification:

- It is certainly possible there are more cases but they may not have been filed with the program if they did not meet our severity requirements. To receive compensation one must have symptoms six months after the vaccine or be hospitalized with a surgery. (b) (5)
- I am still working on the SIRVA numbers
- The data we have goes back to 1988 and this is what I provided but I need to verify that the older data is accurate and reliable. The data is from the 2000's onward is very accurate.
- I was surprised by the number of claims conceded for encephalopathy. The majority were in the 1990's. We have only had (b) (6) claims paid out since 2011. (b) (5)
- I am working on obtaining the number of doses of vaccine distributed. I know that between number of doses of vaccines (covered by the VICP) distributed in the U.S. from 01/01/2006 through 12/31/2017 was 3,454,269,356. I am going to attempt to get a number for the timeframe of 1988-2017 as that will align with our data.

Let me know if I am missing anything or if you have questions.

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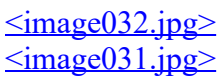 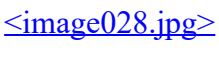 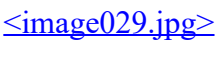 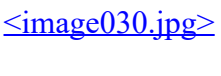

From: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Sent: Saturday, February 02, 2019 4:11 PM
To: 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Perfect for me

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Saturday, February 02, 2019 4:06 PM
To: Stanley Plotkin; 'Nair, Narayan (HRSA)'
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Lets do 11:45 am on Wednesday February 20 if that is okay for Narayan

Cody

From: Stanley Plotkin [stanley.plotkin@vaxconsult.com]
Sent: Saturday, February 02, 2019 3:56 PM
To: Meissner, Cody; 'Nair, Narayan (HRSA)'
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

I should have written February 21st, because I thought you were not available on Feb 20. If Feb 20 is OK it would be easier for me, but if not I will do Feb 21 at 11:45. Sorry for the blunder, please clarify.
Stanley

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Friday, February 01, 2019 4:04 PM
To: 'Stanley Plotkin'; 'Nair, Narayan (HRSA)'
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Fine here

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Friday, February 01, 2019 2:35 PM
To: Meissner, Cody; 'Nair, Narayan (HRSA)'
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

I propose 11:45 February 20. Is that OK?

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Friday, February 01, 2019 2:21 PM
To: 'Stanley Plotkin'
Subject: RE: [EXT] RE: AE events reported to Vaccine Injury Program

Does late morning or noon Feb 21 work?
Feb 20 is full

From: Stanley Plotkin [mailto:stanley.plotkin@vaxconsult.com]
Sent: Friday, February 01, 2019 12:53 PM
To: Meissner, Cody
Subject: [EXT] RE: AE events reported to Vaccine Injury Program

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

Are you unavailable on feb 20 or the morning of feb 21?

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Friday, February 01, 2019 10:49 AM
To: 'Nair, Narayan (HRSA)'; Stanley Plotkin
Subject: RE: AE events reported to Vaccine Injury Program

Thursday Feb 21 at 1:00 or after works for me (boston time)
Cody

From: Nair, Narayan (HRSA) [mailto:NNair@hrsa.gov]
Sent: Friday, February 01, 2019 9:11 AM
To: Stanley Plotkin; Meissner, Cody
Subject: [EXT] RE: AE events reported to Vaccine Injury Program

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

Feb 20 after noon works for me. Feb 21, I am currently free the entire day.

Narayan Nair, MD
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From: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Sent: Friday, February 01, 2019 9:07 AM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>
Subject: RE: AE events reported to Vaccine Injury Program

OK. Are Feb 20 or 21 OK for both of you? If so, let me know which times are NOT OK.
S

From: Nair, Narayan (HRSA) [mailto:NNair@hrsa.gov]
Sent: Friday, February 01, 2019 9:04 AM
To: Stanley Plotkin; 'Meissner, Cody'
Subject: RE: AE events reported to Vaccine Injury Program

I think a conference call in 2 weeks would work for me.

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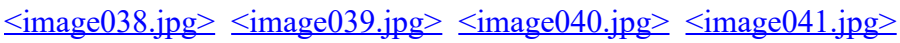


From: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Sent: Friday, February 01, 2019 8:31 AM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>
Subject: RE: AE events reported to Vaccine Injury Program

Dear Narayan and Cody:

I will be going overseas next Tuesday for two weeks. Do you think a conference call is needed Monday or Tuesday, or shall I set up a call after my return (for example February 20), presuming that Narayan will have some figures on the number of awards for specific vaccine reactions? Please respond asap.

Stanley

From: Nair, Narayan (HRSA) [mailto:NNair@hrsa.gov]
Sent: Thursday, January 31, 2019 1:07 PM
To: Stanley Plotkin; 'Meissner, Cody'
Subject: RE: AE events reported to Vaccine Injury Program

I am back on line and happy to discuss next steps for this project.

Narayan Nair, MD
CAPT, USPHS
Division Director
Division of Injury Compensation Programs
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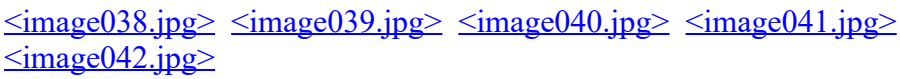

From: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Sent: Monday, January 28, 2019 5:15 PM
To: 'Meissner, Cody' <cmeissner@tuftsmedicalcenter.org>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: AE events reported to Vaccine Injury Program

A great start. Narayan, when will you be online again?
Stanley

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Monday, January 28, 2019 2:07 PM
To: 'Stanley Plotkin'; 'Nair, Narayan (HRSA)'
Subject: AE events reported to Vaccine Injury Program

As follow-up to the conversation between Stanley and myself, this is a suggested list of AE for which it may be possible to get incidence rates after vaccination based on claims filed. Estimated background rates for encephalopathy/encephalitis, arthritis, thrombocytopenia, GBS are reasonably easy to determine.
Cody

Adverse Reactions Recognized in the Vaccine Injury Table

1. Vaccines containing cellular pertussis antigens or tetanus toxoids
    a. Anaphylaxis

    b. Shoulder injury related to vaccine administration
2. Vaccines containing MMRV
    a. Encephalopathy or encephalitis (vaccine associated acute disseminated encephalomyelitis)
    b. Chronic arthritis
    c. Thrombocytopenic purpura
3. Rotavirus vaccines
    a. Intussusception
4. Influenza vaccines
    a. Guillain-Barre syndrome (also MMR, HPV, meningococcal vaccines)

This is a suggestion of conditions recognized in the Table that are not related to vaccine handling or vaccine administration. The number of certain conditions (such as GBS, encephalopathy, arthritis, thrombocytopenia) for which claims were filed and awarded could be determined over a certain period. This number could be normalized based on the number of vaccines distributed during the same time period and the rate could be compared with figures in the literature for each condition.

Issues will be how accurately the filed claims represent the true number, getting an accurate estimate of vaccine doses distributed, assigning a background rate of occurrence of each condition, standardizing definitions in the literature with those in the vaccine injury table and the Brighton definition.

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From: Stanley Plotkin
To: Rubin, Mary (HRSA); "Meissner, Cody"; Nair, Narayan (HRSA)
Subject: RE: Dravet Syndrome
Date: Friday, May 03, 2019 10:30:37 AM

I would just comment that the Dravet situation is illustrative of the problem with the compensation system: it vacillates between science and the need to satisfy the public that putative reactions will be compensated. It also illustrates how growth of knowledge can change our understanding. Getting this across to the public is difficult and the WSJ article is a great attempt to do this. I agree that a paper should bring attention to the science but should also review how many cases of Dravet have been compensated and how many not as an illustration of the problem.
Stanley

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Thursday, May 02, 2019 4:16 PM
To: Meissner, Cody; Nair, Narayan (HRSA)
Cc: Stanley Plotkin
Subject: RE: Dravet Syndrome

Hi Cody,

Sorry for the delay. (b) (5) There are published decisions on Dravet which we can point to but they caution giving case specific details in the paper for confidentiality purposes. I will also have to get ethics clearance if we go ahead with this.

(b) (5) If we were to go ahead with this paper, I would like to inform them that this is happening. I'm not sure if they would be interested in participating but at the very least they can be very good resources.

On a related note, thank you for the email regarding the WSJ post on Dravets and Vaccines.

(b) (5) attached those for your information.

Happy to discuss further,

Mary

From: Rubin, Mary (HRSA)
Sent: Friday, April 26, 2019 4:54 PM
To: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
Cc: Stanley Plotkin <stanley.plotkin@vaxconsult.com>

Subject: RE: Dravet Syndrome

Hi Cody, interesting proposal. (b) (5) and get back to you.

Mary

From: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Sent: Thursday, April 18, 2019 1:13 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
Cc: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Subject: RE: Dravet Syndrome

Dear Mary,
Thank you for providing this information.
This syndrome seems to be well known among neurologists, unlike ID community.
Your data are quite interesting.
One question for you and Narayan and Stanley, do you think this data regarding this syndrome (I am learning other neuronal Na+ channel defects can lead to similar syndrome) would be of interest in a publication, particularly as it relates to immunization? From my limited discussions, there seems to be misunderstanding of this issue.
Cody

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Thursday, April 18, 2019 9:07 AM
To: Nair, Narayan (HRSA); Meissner, Cody
Cc: Stanley Plotkin
Subject: [EXT] RE: Dravet Syndrome

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

Hi Cody,

Thanks for the email and great question. (b) (5) To date, we have (b) (6), claims of confirmed or suspected Dravet syndrome. (b) (6), (b) (3) (of the (b) (6), (b went to hearing, and in all (b) (, the Special Master (SM) denied entitlement (did not find causal association with the vaccine). (b) (6), (b) (3) (A) were appealed to the higher courts, with the judges from the higher courts affirming the decision of the SM. (b) (6), (b) (3 of these cases went to the Federal circuit which are binding decisions. These decisions were finalized in 2011-2012. The cases that followed after those CFC decisions were then dismissed (b) (6) cases). (b) (6), (b) (3) (A) (b) (6), (b) (3

(b) (6), (b) (3) (b) (5)

(b) (5)

Hope I answered your question. Pls. let me know if you'd like more information.

Best,
Mary

Mary Nythel Rubin, MD
Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
Department of Health and Human Services
mrubin@hrsa.gov
(301)443-4047

From: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Sent: Tuesday, April 16, 2019 8:39 AM
To: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Cc: Stanley Plotkin <stanley.plotkin@vaxconsult.com>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: Re: Dravet Syndrome

Thanks Cody for this information. I have cc'ed Dr. Mary Rubin. She is our Chief Medical Officer and is very familiar with our claims involving Dravet's. She can provide you some additional information about how we handle these cases.

Sent from my iPhone

On Apr 15, 2019, at 2:28 PM, Meissner, Cody <cmeissner@tuftsmedicalcenter.org> wrote:

> Dear Narayan and Stanley,
> During a recent conference with pediatric neurologists, the issue of vaccine complications and Vaccine Injury Compensation awards came up.
> I was surprised to hear that the neurologists felt a number of awards had gone to patients with Dravet Syndrome but the diagnosis had not been made.
> Being unfamiliar with this syndrome, I found it is a rare, genetically determined disease consisting of seizures, developmental delay, loss of milestones and behavior problems (autism like) that begin early in life around 6 to 12 months of age in previously healthy

children.
Fever is an important trigger for onset of syndrome. The point being that a febrile reaction to a vaccine may initiate the syndrome but that the syndrome would occur subsequently with any febrile reaction.
The mutated genes are involved in sodium channel transport in a specific set of neurons.
The diagnosis is established by screening for the genotype and there is variable penetrance resulting in a spectrum of disease expression,
The neurologists felt this genetic disease may account for at least some of the claims brought against vaccines.
Narayan, has this been considered?
If not, could this be investigated?
Couple references attached.
Regards,
Cody

<Dravet 8.pdf>

<Dravet 2.pdf>

<Dravet 4a.pdf>

The information in this e-mail is intended only for the person to whom it is addressed. If you believe this e-mail was sent to you in error and the e-mail contains patient information, please contact the Tufts Medical Center HIPAA Hotline at (617) 636-4422. If the e-mail was sent to you in error but does not contain patient information, contact the sender and properly dispose of the e-mail.

Please consider the environment and the security of the information contained within or attached to this e-mail before printing or saving to an insecure location.

From: Stanley Plotkin
To: "Meissner, Cody"; Rubin, Mary (HRSA); Nair, Narayan (HRSA)
Subject: RE: Dravet Syndrome
Date: Friday, May 03, 2019 2:43:39 PM

Cody and Nair, I'd like to be clear on one point: children with Dravet syndrome have had awards, right?
Stanley

From: Meissner, Cody [mailto:cmeissner@tuftsmedicalcenter.org]
Sent: Friday, May 03, 2019 1:35 PM
To: 'Rubin, Mary (HRSA)'; Nair, Narayan (HRSA)
Cc: Stanley Plotkin
Subject: RE: Dravet Syndrome

Since we can address the issue of rate of Dravet syndrome, this could be included in Narayan's paper .
Alternatively, as Stanley notes, there are several important points here that could be developed as a separate paper.
Comments?
Cody

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Thursday, May 02, 2019 4:16 PM
To: Meissner, Cody; Nair, Narayan (HRSA)
Cc: Stanley Plotkin
Subject: [EXT] RE: Dravet Syndrome

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

Hi Cody,

Sorry for the delay. (b) (5) (b) (5) There are published decisions on Dravet which we can point to but they caution giving case specific details in the paper for confidentiality purposes. I will also have to get ethics clearance if we go ahead with this.

(b) (5) f we were to go ahead with this paper, I would like to inform them that this is happening. I'm not sure if they would be interested in participating but at the very least they can be very good resources.

On a related note, thank you for the email regarding the WSJ post on Dravets and Vaccines.

(b) (5)
I've attached those for your information.

Happy to discuss further,

Mary

From: Rubin, Mary (HRSA)
Sent: Friday, April 26, 2019 4:54 PM
To: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
Cc: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Subject: RE: Dravet Syndrome

Hi Cody, interesting proposal. (b) (5) and get back to you.

Mary

From: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Sent: Thursday, April 18, 2019 1:13 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>; Nair, Narayan (HRSA) <NNair@hrsa.gov>
Cc: Stanley Plotkin <stanley.plotkin@vaxconsult.com>
Subject: RE: Dravet Syndrome

Dear Mary,
Thank you for providing this information.
This syndrome seems to be well known among neurologists, unlike ID community.
Your data are quite interesting.
One question for you and Narayan and Stanley, do you think this data regarding this syndrome (I am learning other neuronal Na+ channel defects can lead to similar syndrome) would be of interest in a publication, particularly as it relates to immunization? From my limited discussions, there seems to be misunderstanding of this issue.
Cody

From: Rubin, Mary (HRSA) [mailto:MRubin@hrsa.gov]
Sent: Thursday, April 18, 2019 9:07 AM
To: Nair, Narayan (HRSA); Meissner, Cody
Cc: Stanley Plotkin
Subject: [EXT] RE: Dravet Syndrome

EXTERNAL MESSAGE - TREAT LINKS/FILES WITH CARE

Hi Cody,

Thanks for the email and great question. [redacted] date, we have [redacted] claims of confirmed or suspected Dravet syndrome. [redacted] of the [redacted] went to hearing, and in all [redacted], the Special Master (SM) denied entitlement (did not find causal association with the vaccine). [redacted] were appealed to the higher courts, with the judges from the higher courts affirming the decision of the SM. [redacted] of these cases went to the Federal circuit which are binding decisions. These decisions were finalized in 2011-2012. The cases that followed after those CFC decisions were then dismissed [redacted] cases). [redacted]

Hope I answered your question. Pls. let me know if you'd like more information.

Best,
Mary

Mary Nythel Rubin, MD
Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
Department of Health and Human Services
mrubin@hrsa.gov
(301)443-4047

From: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Sent: Tuesday, April 16, 2019 8:39 AM
To: Meissner, Cody <cmeissner@tuftsmedicalcenter.org>
Cc: Stanley Plotkin <stanley.plotkin@vaxconsult.com>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: Re: Dravet Syndrome

Thanks Cody for this information. I have cc'ed Dr. Mary Rubin. She is our Chief Medical Officer and is

very familiar with our claims involving Dravet's. She can provide you some additional information about how we handle these cases.

Sent from my iPhone

On Apr 15, 2019, at 2:28 PM, Meissner, Cody <cmeissner@tuftsmedicalcenter.org> wrote:

> Dear Narayan and Stanley,
> During a recent conference with pediatric neurologists, the issue of vaccine complications and Vaccine Injury Compensation awards came up.
> I was surprised to hear that the neurologists felt a number of awards had gone to patients with Dravet Syndrome but the diagnosis had not been made.
> Being unfamiliar with this syndrome, I found it is a rare, genetically determined disease consisting of seizures, developmental delay, loss of milestones and behavior problems (autism like) that begin early in life around 6 to 12 months of age in previously healthy children.
> Fever is an important trigger for onset of syndrome. The point being that a febrile reaction to a vaccine may initiate the syndrome but that the syndrome would occur subsequently with any febrile reaction.
> The mutated genes are involved in sodium channel transport in a specific set of neurons.
> The diagnosis is established by screening for the genotype and there is variable penetrance resulting in a spectrum of disease expression,
> The neurologists felt this genetic disease may account for at least some of the claims brought against vaccines.
> Narayan, has this been considered?
> If not, could this be investigated?
> Couple references attached.
> Regards,
> Cody
>
>
>
> <Dravet 8.pdf>
> <Dravet 2.pdf>
> <Dravet 4a.pdf>

you in error but does not contain patient information, contact the sender and properly dispose of the e-mail.

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Please consider the environment and the security of the information contained within or attached to this e-mail before printing or saving to an insecure location.

From: Nair, Narayan (HRSA)
To: Overby, Tamara (HRSA); Rubin, Mary (HRSA)
Subject: RE: **ACTION REQUIRED** Quarterly Travel & Conference Data Call: April-June 2019 - DUE Wednesday, February 6 @ 4pm
Date: Sunday, January 27, 2019 11:14:49 AM
Attachments: image001.png

No changes to this at this time. I think we both were going to try and attend CISA. It would be helpful to have 1 pediatrician and 1 adult physician there.

Narayan Nair, MD
CAPT, USPHS
Division Director
Division of Injury Compensation Programs
Healthcare Systems Bureau
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5600 Fishers Lane, Room 8N23
Rockville, MD 20857

HRSA

From: Overby, Tamara (HRSA) <TOverby@hrsa.gov>
Sent: Friday, January 25, 2019 5:11 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: FW: **ACTION REQUIRED** Quarterly Travel & Conference Data Call: April-June 2019 - DUE Wednesday, February 6 @ 4pm

Hi Narayan and Mary,
Please see the request below. For April – June, the following trips have already been entered into the travel request system.
Narayan to ACIP in June, CISA in April and NVAC in June
Mary to CISA in April
Are there any changes to these request? Are both of you planning to attend CISA in April?

Tamara Overby, MBA
Deputy Director, Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
Department of Health and Human Services
5600 Fishers Lane, Room 08N-142
Rockville, MD 20857
Telephone: 301-443-3766
Cell: (b) (6)
E-mail: toverby@hrsa.gov

HRSA

From: Lowery, Kimberly (HRSA) <KLowery@hrsa.gov>
Sent: Friday, January 25, 2019 12:17 PM
To: Pedley, Krista (HRSA) <KPedley@hrsa.gov>; Herzog, Michelle (HRSA) <MHerzog@hrsa.gov>; Nair, Narayan (HRSA) <NNair@hrsa.gov>; Overby, Tamara (HRSA) <TOverby@hrsa.gov>; Holloman, Frank (HRSA) <FHolloman@hrsa.gov>; Germain, Mesmin (HRSA) <MGermain@hrsa.gov>; Grant, Shelley (HRSA) <SGrant@hrsa.gov>; Pickett, Jeri (HRSA) <JPickett@hrsa.gov>; Tracy, Kevin (HRSA) <KTracy@hrsa.gov>; Hue, Michael (HRSA) <MHue@hrsa.gov>; Stevenson, Sondra (HRSA) <SStevenson1@hrsa.gov>
Cc: Felton, Brad (HRSA) <BFelton@hrsa.gov>; Proctor, Gwendolyn (HRSA) <GProctor@hrsa.gov>; Duarte, Tammy (HRSA) <TDuarte@hrsa.gov>; Tongele, Passy (HRSA) <PTongele@hrsa.gov>
Subject: **ACTION REQUIRED** Quarterly Travel & Conference Data Call: April-June 2019 - DUE Wednesday, February 6 @ 4pm

Good afternoon, HSB,

The 3rd quarter travel data call is due by **4pm on Wednesday, February 6th.** Please submit any new travel requests and verify that existing requests are accurate. Any changes to or cancellations of existing requests should come to me. All requests need to be in "*Pending FATA Verification*" status by the due date.

Please let Tammy or me know if you have any questions. Thank you!

Kim Lowery, Management Analyst
Ph. (301) 945-9822

From: HRSA Travel <HRSATravel@hrsa.gov>
Sent: Friday, January 25, 2019 10:14 AM
To: HRSA Travel <HRSATravel@hrsa.gov>
Subject: **ACTION REQUIRED** Quarterly Travel & Conference Data Call: April-June 2019

Good morning,

Bureaus should begin entry of all travel requests for **April 1, 2019 – June 30, 2019** in **STARS**. STARS requests with 'event type' labeled conference will automatically route to OAM for review and approval in STARS. As a reminder, the following travel requests must be marked for OAM review and approval in STARS:

- All OCONUS travel requests
- All travel requests with costs greater than $3,000.00 per traveler
- All travel requests with 3 or more people traveling
- All invitational travel requests
- Site visits involving 4 or more people (non-grant related)

Traveler justifications are required for all requests that will be routed to OAM.

Note: If your Office/Bureau will be hosting/sponsoring a conference, you will need to complete the attached *HRSA Hosted Conference Request and Approval* ***Form***; as well as provide an agenda and an Independent Government Cost Estimate (**IGCE**) to the Office of Administration Management for review/approval. If you need more information regarding this process, contact **HRSATravel@hrsa.gov**.

Thank you,
HRSA Travel Team
HRSA Travel SharePoint Site

From:	Nair, Narayan (HRSA)
To:	Atanasoff, Sarah (HRSA); Dalle-Tezze, Terry (HRSA); Ditmar, Mark (HRSA); Luna, Kenneth (HRSA); Melo, Marco (HRSA); Osborn, Mark (HRSA); Rubin, Mary (HRSA); Sisk, Nasrin (HRSA); St. Martin, Laura (HRSA); Stryer, Stacy (HRSA)
Subject:	ACIP notes
Date:	Tuesday, October 30, 2018 12:11:39 PM
Attachments:	image001.png agenda-2018-10-508.pdf

Good morning,

I attended the ACIP last week. Here is a very brief summary. I have attached the full agenda. Please let me know if you want more details as I have detailed notes I can share.

- The committee passed a vote stating that all persons aged 1 year and older experiencing homelessness should be routinely immunized against hepatitis A
- A rabies working group was created at the session
- Changes were made to the adult and adolescent/children vaccination schedule to make it accessible online and more user-friendly
- HPV and POI: A study of nearly 200, 000 young women, observed no evidence of increased risk of POI following the HPV vaccination or other routine adolescent exposures. This should lessen the concerns about fertility and other routine vaccinations. (I sent this study out a while ago)
- Numerous advocates participated in public comment sessions both days with statements. Most were parents and stated that vaccines had caused their children's autism, ADEM, cancer, suicide, and other conditions. They were highly critical of CDC, FDA and VICP.

Narayan Nair, MD
CAPT, USPHS
Division Director
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
5600 Fishers Lane, Room 8N23
Rockville, MD 20857

HRSA

Final - October 16, 2018

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

Centers for Disease Control and Prevention
1600 Clifton Road, NE, Tom Harkin Global Communications Center, Kent "Oz" Nelson Auditorium
Atlanta, Georgia 30329
October 24-25, 2018

	AGENDA ITEM	PURPOSE	PRESIDER/PRESENTER(s)
Wednesday, October 24			
8:00	**Welcome & Introductions**		Dr. Amanda Cohn (ACIP Executive Secretary; CDC)
8:30	**Hepatitis A Vaccines**		
	Introduction	Information & Discussion	Dr. Kelly Moore (ACIP, WG Chair)
	Background		Dr. Noele Nelson (CDC/NCHHSTP)
	Homelessness as a risk group: Evidence to Recommendation Framework and GRADE		Dr. Mona Doshani (CDC/NCHHSTP)
	Public comment		
	Recommendation vote	**Vote**	Dr. Noele Nelson (CDC/NCHHSTP)
	VFC vote	**VFC Vote**	Dr. Jeanne Santoli (CDC/NCIRD)
10:15	***Break***		
10:30	**Pneumococcal Vaccines**		
	Introduction	Information & Discussion	Dr. Grace Lee (ACIP, WG Chair)
	PCV13 Impact on IPD and serotype distribution for the remaining disease burden		Dr. Tamara Pilishvili (CDC/NCIRD)
	Incidence of non-Invasive Pneumococcal Pneumonia before and after PCV13 recommendation for adults ≥65yo		Mr. Ryan Gierke (CDC/NCIRD)
	U.S. trends in pneumonia hospitalizations		Dr. Fernanda Lessa (CDC/NCIRD)
	Economic analysis of PCV13 for adults ≥65 year old		Dr. Charles Stoecker (Tulane University School of Public Health and Tropical Medicine)
	Preliminary EtR and GRADE. Summary and timeline		Dr. Almea Matanock (CDC/NCIRD)
12:15	***Lunch***		
1:30	**Adult Immunization Schedule**		
	Introduction	Information & Discussion	Dr. Paul Hunter (ACIP, WG Chair)
	Proposed 2019 adult immunization schedule		Dr. David Kim (CDC/NCIRD)
2:20	**Child/Adolescent Immunization Schedule**		
	Introduction	Information & Discussion	Dr. Henry Bernstein (ACIP, WG Chair)
	Proposed 2019 child and adolescent immunization schedule		Dr. Candice Robinson (CDC/NCIRD)
	Public comment		
	Immunization schedules recommendations vote	**Vote**	Drs. David Kim and Candice Robinson (CDC/NCIRD)
3:00	***Break***		
3:15	**Japanese Encephalitis**		
	Introduction	Information & Discussion	Dr. Chip Walter (WG chair)
	JE vaccine Evidence to Recommendations		Dr. Susan Hills (CDC/NCEZID)
	JE-VC accelerated schedule recommendation for adults		Dr. Susan Hills (CDC/NCEZID)
	JE-VC pediatric booster and booster dose recommendations		Dr. Susan Hills (CDC/NCEZID)
	Conclusions and next steps		Dr. Susan Hills (CDC/NCEZID)
4:15	**Anthrax**		
	Introduction	Information	Dr. David Stephens (ACIP, WG Chair)
	NuThrax®		Dr. Paul- Andre de Lame, Mr. Jeff Shearer (Emergent BioSolutions)
	Anthrax antitoxin for PEP		Dr. William Bower (CDC/NCEZID)
5:00	**Vaccine Supply**		
5:05	**Public Comment**		
5:20	**Adjourn**		

Thursday, October 25

8:00	**Agency Updates & Unfinished Business**		
	CDC, CMS, DoD, DVA, FDA, HRSA, IHS, NIH, NVPO	Information	Dr. Nancy Messonnier (CDC/NCIRD); *Ex Officio* Members
8:30	**Human Papillomavirus**		
	Introduction		Dr. Peter Szilagyi (ACIP, WG Chair)
	Vaccine safety update - no association with primary ovarian insufficiency		Ms. Julianne Gee (CDC/NCEZID)
	Background - Expanded age indication for 9vHPV	Information & Discussion	Dr. Lauri Markowitz (CDC/NCIRD)
	GRADE		Dr. Elissa Meites (CDC/NCIRD)
	Impact and economic analyses		Dr. Harrell Chesson (CDC/NCHHSTP)
	Recommendation options		Dr. Lauri Markowitz (CDC/NCIRD)
10:15	***Break***		
10:45	**General Recommendations**		
	Introduction		Dr. Paul Hunter (ACIP, WG Chair)
	Background and posted changes since April 2017	Information & Discussion	Dr. Andrew Kroger (CDC/NCIRD)
	Vaccine Administration – Vaccinators with conditions that are contraindications or precautions		Dr. Andrew Kroger (CDC/NCIRD)
11:15	**Influenza**		
	Introduction		Dr. Chip Walter
	Influenza vaccine effectiveness in preventing influenza-associated hospitalizations during pregnancy	Information & Discussion	Dr. Mark Thompson (CDC/NCIRD)
	Fluzone Quadrivalent 0.5-mL dose for children aged 6 through 35 Months		Dr. Monica Mercer (Sanofi Pasteur)
12:15	**Rabies**		
	Workgroup update	Information	Dr. Sharon Frey (ACIP, WG Chair)
12:20	**Meningococcal**		
	Workgroup Update	Information	Dr. David Stephens (ACIP, WG Chair)
12:25	**Pertussis**		
	Introduction to Work Group		Dr. Henry Bernstein (ACIP, WG Chair)
	Background to current ACIP recommendations (Td and Tdap) and policy considerations for Tdap revaccination	Information	Dr. Fiona Havers (CDC/NCIRD)
	Adacel revaccination safety and immunogenicity		Dr. David Greenberg (Sanofi Pasteur)
	Boostrix revaccination safety and immunogenicity		Dr. Leonard Silverstein (GSK)
1:30	**Public Comment**		
1:45	**Adjourn**		

Acronyms

9vHPV	9-Valent Human Papillomavirus Vaccine
CDC	Centers for Disease Control & Prevention
CMS	Centers for Medicare and Medicaid Services
DoD	Department of Defense
DVA	Department of Veterans Affairs
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HRSA	Health Resources and Services Administration
IHS	Indian Health Service
IPD	Invasive pneumococcal disease
JE-VC	Vero cell culture-derived Japanese encephalitis vaccine
NCHHSTP	National Center for HIV, Hepatitis, STD and TB Prevention [of CDC/OID]
NCIRD	National Center for Immunization & Respiratory Diseases [of CDC/OID]
NCEZID	National Center for Emerging and Zoonotic Diseases [of CDC/OID]
NVPO	National Vaccine Program Office
PEP	Post-exposure prophylaxis
PCV13	13-valent pneumococcal conjugate vaccine
Td	Tetanus and diphtheria vaccine
Tdap	Tetanus, diphtheria, and pertussis vaccine
VFC	Vaccines for Children
WG	Work Group

From: Nair, Narayan (HRSA)
To: Rubin, Mary (HRSA)
Subject: RE: ACIP Draft Agenda, June 2018
Date: Thursday, June 21, 2018 8:44:15 AM

Sorry, I didn't get a chance to update the numbers. Unfortunately, we have to get clearance even if we change just the numbers.

Narayan Nair, MD
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From: Rubin, Mary (HRSA)
Sent: Wednesday, June 20, 2018 12:08 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: ACIP Draft Agenda, June 2018

Thanks, Narayan. If those updated numbers have been cleared for presentation and if giving those numbers don't disrupt the flow of ACIP updates – I would like to present them. But if it is not cleared for presentation – I'll go with what I have. I just saw the website and it was updated June 4, 2014 so that's why I wondered why I had April numbers.

From: Nair, Narayan (HRSA)
Sent: Wednesday, June 20, 2018 12:03 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: ACIP Draft Agenda, June 2018

It takes a while to get these presentations cleared so that is why it was the April numbers. Even these brief updates have to be cleared and when I submitted this one for clearance these were the most up to date numbers I had. Do you want to present more up to date ones. I think I have those numbers.

Narayan Nair, MD
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Telephone: 301-443–5287
Fax: 301-443-0704
E-mail: nnair@hrsa.gov

From: Rubin, Mary (HRSA)
Sent: Wednesday, June 20, 2018 11:43 AM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: ACIP Draft Agenda, June 2018

Hi Narayan,

Hope you had a nice (b) (6)! Question – what's the reason that numbers are as of April 30? Is it a quarterly summary?

Thanks!

Mary

From: Nair, Narayan (HRSA)
Sent: Thursday, May 10, 2018 3:17 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: FW: ACIP Draft Agenda, June 2018

Good afternoon Mary,

I have attached the update you will be giving at ACIP. Basically you just read what is written. Below is a link to the October meeting video. At about the 4 minute mark you can see the VICP update. This gives you a flavor for how it works.

https://www.youtube.com/watch?v=paBNPKNxuxE

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Telephone: 301-443–5287
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From: Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Sent: Wednesday, May 09, 2018 3:44 PM
To: Deussing, Eric (CDC/OPHPR/OD) <ncu0@cdc.gov>; Hance, Mary Beth E. (CMS/CMCS) <marybeth.hance@cms.hhs.gov>; Jane Kim <Jane.Kim3@va.gov>; Mulach, Barbara (NIH/NIAID) [E] <bmulach@niaid.nih.gov>; Nair, Narayan (HRSA) <NNair@hrsa.gov>; Sun, Wellington (FDA/CBER) <wellington.sun@fda.hhs.gov>; McCollum, Jeffrey T (IHS/HQ) <Jeffrey.McCollum@ihs.gov>; Wharton, Melinda (CDC/OID/NCIRD) <mew2@CDC.GOV>
Subject: ACIP Draft Agenda, June 2018

Hello all,

Attached is the draft agenda for the upcoming ACIP meeting.

Please register for the meeting if you haven't already:

https://www2a.cdc.gov/vaccines/acip/juneregistration.asp

See you soon,

Stephanie

Stephanie B. Thomas

Management Analyst/Committee Management Specialist
Advisory Committee on Immunization Practices (ACIP)
National Center for Immunization and Respiratory Diseases (NCIRD)
Office of the Director (OD)
Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/vaccines/acip/index.html
Office: 404-639-8367/Mobile: 404-610-0509
Mailing address: 1600 Clifton Road NE/MS-A27/Atlanta, GA 30329-4027

From: Nair, Narayan (HRSA)
To: Rubin, Mary (HRSA)
Subject: RE: ACIP Background Materials, June 2018
Date: Thursday, June 14, 2018 2:19:30 PM

I am at home so call (b) (6)

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Telephone: 301-443–5287
Fax: 301-443-0704
E-mail: nnair@hrsa.gov

From: Rubin, Mary (HRSA)
Sent: Thursday, June 14, 2018 2:19 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: ACIP Background Materials, June 2018

Hi Narayan,
I can talk now.
I'll call your work phone?
Mary

From: Nair, Narayan (HRSA)
Sent: Thursday, June 14, 2018 2:12 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: ACIP Background Materials, June 2018

I finished my 2:00 meeting early. Are you free to talk now. Not a problem if you are busy

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From: Rubin, Mary (HRSA)
Sent: Wednesday, June 13, 2018 10:45 AM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: ACIP Background Materials, June 2018

Thanks for sending. I didn't get it.
I registered in March and my travel is set. Do I need to sign in or anything when I get there? I got the attached email yesterday – there's a note about Public comment – does that apply to me (so I can provide ACIP update)?
Mary

From: Nair, Narayan (HRSA)
Sent: Wednesday, June 13, 2018 10:40 AM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: FW: ACIP Background Materials, June 2018
Hello Mary, not sure if you got one of these messages.
Narayan Nair, MD
CAPT, USPHS
Division Director/Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
5600 Fishers Lane, Room 8N23
Rockville, MD 20857
Telephone: 301-443–5287
Fax: 301-443-0704
E-mail: nnair@hrsa.gov

From: Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Sent: Wednesday, June 13, 2018 10:34 AM
To: Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Subject: ACIP Background Materials, June 2018
Hello all,
ACIP has decided to use ShareFile to share background materials with you for this meeting and all future meetings. It is very user friendly and straightforward, just click the link below to access the saved files.
Please do not share this link with anyone who is not part of the ACIP membership except for a person who is attending the meeting in your place.
I will be uploading the meeting presentation files to this same site, once I receive them (there aren't any yet).
https://centersfordiseasecontrol (b) (5)
Please let me know if you have issues or questions.
Thanks!
Stephanie

Stephanie B. Thomas
Management Analyst/Committee Management Specialist
Advisory Committee on Immunization Practices (ACIP)
National Center for Immunization and Respiratory Diseases (NCIRD)
Office of the Director (OD)
Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/vaccines/acip/index.html
Office: 404-639-8367/Mobile: 404-610-0509

From: Nair, Narayan (HRSA)
To: Rubin, Mary (HRSA)
Subject: RE: ACIP Background Materials, June 2018
Date: Wednesday, June 13, 2018 1:14:35 PM

No you are an ex-officio member so you don't need to worry about the public comment. Let's try and talk tomorrow to make sure you have everything you need. What is a good time?

Narayan Nair, MD
CAPT, USPHS
Division Director/Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
5600 Fishers Lane, Room 8N23
Rockville, MD 20857
Telephone: 301-443–5287
Fax: 301-443-0704
E-mail: nnair@hrsa.gov

From: Rubin, Mary (HRSA)
Sent: Wednesday, June 13, 2018 10:45 AM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: ACIP Background Materials, June 2018

Thanks for sending. I didn't get it.
I registered in March and my travel is set. Do I need to sign in or anything when I get there? I got the attached email yesterday – there's a note about Public comment – does that apply to me (so I can provide ACIP update)?
Mary

From: Nair, Narayan (HRSA)
Sent: Wednesday, June 13, 2018 10:40 AM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: FW: ACIP Background Materials, June 2018

Hello Mary, not sure if you got one of these messages.

Narayan Nair, MD
CAPT, USPHS
Division Director/Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration
5600 Fishers Lane, Room 8N23
Rockville, MD 20857
Telephone: 301-443–5287
Fax: 301-443-0704
E-mail: nnair@hrsa.gov

From: Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Sent: Wednesday, June 13, 2018 10:34 AM

To: Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Subject: ACIP Background Materials, June 2018

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Please do not share this link with anyone who is not part of the ACIP membership except for a person who is attending the meeting in your place.

I will be uploading the meeting presentation files to this same site, once I receive them (there aren't any yet).

https://centersfordiseasecontrol. (b) (5)

Please let me know if you have issues or questions.

Thanks!

Stephanie

Stephanie B. Thomas
Management Analyst/Committee Management Specialist
Advisory Committee on Immunization Practices (ACIP)
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Mailing address: 1600 Clifton Road NE/MS-A27/Atlanta, GA 30329-4027

From: Nair, Narayan (HRSA)
To: Rubin, Mary (HRSA); Dalle-Tezze, Terry (HRSA)
Subject: RE: Vaccines and the U.S. Mystery of Acute Flaccid Myelitis | The BMJ
Date: Thursday, May 31, 2018 10:44:21 AM

I have not heard of this being discussed in NVAC or ACIP.

Narayan Nair, MD
CAPT, USPHS
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Division of Injury Compensation Programs
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Telephone: 301-443–5287
Fax: 301-443-0704
E-mail: nnair@hrsa.gov

From: Rubin, Mary (HRSA)
Sent: Wednesday, May 30, 2018 12:15 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; Dalle-Tezze, Terry (HRSA) <TDalle-Tezze@hrsa.gov>
Subject: FW: Vaccines and the U.S. Mystery of Acute Flaccid Myelitis | The BMJ

Hi Narayan and Terry,

FYI - below is a response to an article in BMJ. It summarizes the theory brought up by our expert Dr. Gorman regarding AFM.

Narayan – have you heard of provocation poliomyelitis mentioned at CDC or NVAC etc…

Mary

From: Camille Collett [mailto:camillecollett@me.com]
Sent: Wednesday, May 30, 2018 12:03 PM
To: Collett, Camille M. (CIV) <ccollett@CIV.USDOJ.GOV>
Subject: Vaccines and the U.S. Mystery of Acute Flaccid Myelitis | The BMJ

https://www.bmj.com/content/350/bmj.h308/rr

Vaccines and the U.S. Mystery of Acute Flaccid Myelitis

Since August 2, 2014 our Centers for Disease Control has received reports of 107 cases of 'acute flaccid myelitis' (AFM), a polio-like illness in children in 34 states. During the same interval there have been 1153 cases of respiratory illnesses associated with enterovirus D-68 (CIDRAP News 1/16/15. CDC update 1/15/15. Catherine Saint Louis, NY Times 1/13/15). AFM affects motor neurons in spinal cord gray matter, resulting in asymmetrical limb weakness;

34% of patients have cranial nerve motor dysfunction. Median age of patients is 7.6 years/range: 5 months-20 years (MMWR 63: 1243--January 9, 2015). So far only one child has fully recovered. EV-D68 is a suspected cause but, thus far, no viruses have been found in the spinal fluid of patients, and only a minority have had an antecedent illness associated with EV-D68. Case-control studies are planned to look for clues, but presently AFM is a mystery disease of unknown cause.

It is taboo to suggest a role for vaccines, but some old-timers remember "provocation poliomyelitis" or "provocation paralysis." This is paralytic polio following intramuscular injections, typically with vaccines. PP was most convincingly documented by Austin Bradford Hill and J. Knowelden during the 1949 British polio epidemic when the risk of paralytic polio was increased 20-fold among children who had received the DPT injection (BMJ 2:1--July 1, 1950). Similar observations were made by Greenberg and colleagues in New York City; their literature review cited suspected cases as far back as 1921 (Am J Public Health 42:142--Feb.1952). I first became aware of PP 10 years ago while browsing through "Krugman's Infectious Disease of Children" (page 128 of the 2004 edition).

AFM may result from a direct virus attack on the spinal cord, or by an immune attack triggered by a virus, or by something else. If a polio-like virus is circulating in the U.S., the possibility of its provocation by one or more vaccines has to be considered.

Sent from my iPhone

From: Nair, Narayan (HRSA)
To: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD)
Cc: Rubin, Mary (HRSA)
Subject: RE: ACIP Draft Agenda, June 2018
Date: Wednesday, May 09, 2018 3:51:08 PM

Thanks Stephanie,
Dr. Mary Rubin from our office will be attending this ACIP meeting in my place. I have cc'ed her on the email.

Narayan Nair, MD
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From: Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Sent: Wednesday, May 09, 2018 3:44 PM
To: Deussing, Eric (CDC/OPHPR/OD) <ncu0@cdc.gov>; Hance, Mary Beth E. (CMS/CMCS) <marybeth.hance@cms.hhs.gov>; Jane Kim <Jane.Kim3@va.gov>; Mulach, Barbara (NIH/NIAID) [E] <bmulach@niaid.nih.gov>; Nair, Narayan (HRSA) <NNair@hrsa.gov>; Sun, Wellington (FDA/CBER) <wellington.sun@fda.hhs.gov>; McCollum, Jeffrey T (IHS/HQ) <Jeffrey.McCollum@ihs.gov>; Wharton, Melinda (CDC/OID/NCIRD) <mew2@CDC.GOV>
Subject: ACIP Draft Agenda, June 2018

Hello all,
Attached is the draft agenda for the upcoming ACIP meeting.
Please register for the meeting if you haven't already:
https://www2a.cdc.gov/vaccines/acip/juneregistration.asp
See you soon,
Stephanie

Stephanie B. Thomas
Management Analyst/Committee Management Specialist
Advisory Committee on Immunization Practices (ACIP)
National Center for Immunization and Respiratory Diseases (NCIRD)
Office of the Director (OD)
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Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 67 / No. 2
April 27, 2018

Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

HRSA000054

CONTENTS

CDC Adoption of ACIP Recommendations for *MMWR* Recommendations and Reports, *MMWR* Policy Notes, and Immunization Schedules (Child/Adolescent, Adult)

Recommendations for routine use of vaccines in children, adolescents, and adults are developed by the Advisory Committee on Immunization Practices (ACIP). ACIP is chartered as a federal advisory committee to provide expert external advice and guidance to the Director of CDC on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in children and adolescents are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG). Recommendations for routine use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, and the American College of Physicians (ACP). ACIP recommendations approved by the CDC Director become agency guidelines on the date published in the *Morbidity and Mortality Weekly Report* (*MMWR*). Additional information is available at https://www.cdc.gov/vaccines/acip.

The *MMWR* series of publications is published by the Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Title]. MMWR Recomm Rep 2018;67(No. RR-#):[inclusive page numbers].

Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

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Tejpratap Tiwari, MD[1]
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[5]*University of California, San Diego; La Jolla, California*
[6]*Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC*

Summary

This report compiles and summarizes all recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) regarding prevention and control of tetanus, diphtheria, and pertussis in the United States. As a comprehensive summary of previously published recommendations, this report does not contain any new recommendations and replaces all previously published reports and policy notes; it is intended for use by clinicians and public health providers as a resource. ACIP recommends routine vaccination for tetanus, diphtheria, and pertussis. Infants and young children are recommended to receive a 5-dose series of diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccines, with one adolescent booster dose of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine. Adults who have never received Tdap also are recommended to receive a booster dose of Tdap. Women are recommended to receive a dose of Tdap during each pregnancy, which should be administered from 27 through 36 weeks' gestation, regardless of previous receipt of Tdap. After receipt of Tdap, adolescents and adults are recommended to receive a booster tetanus and diphtheria toxoids (Td) vaccine every 10 years to assure ongoing protection against tetanus and diphtheria.

Introduction

This report compiles and summarizes all previously published recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) regarding prevention and control of pertussis, tetanus, and diphtheria in the United States, specifically after the introduction of acellular pertussis vaccines, and does not contain any new recommendations. A timeline of ACIP recommendations for DTaP and Tdap during 1991–2015 is available at https://stacks.cdc.gov/view/cdc/52821. This report describes the process undertaken and the rationale used in support of these recommendations and is intended for use by clinicians and public health providers as a resource.

From the late 1940s through the 1990s, vaccination against pertussis, diphtheria, and tetanus with a combined diphtheria and tetanus toxoids and whole-cell pertussis (DTP) vaccine was recommended for infants and young children. Receipt of DTP was commonly associated with local adverse events (e.g., redness, swelling, and pain at the injection site) and less commonly with serious adverse events (*1*,*2*). Because of safety concerns about the whole-cell pertussis component of DTP, diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccines were developed and subsequently replaced doses of DTP in the 1990s. Since 1997, infants and young children have been recommended to receive a 5-dose series of DTaP (*3*). In 2005, ACIP recommended that adolescents and adults receive a single dose of a tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine (*4*,*5*). After receipt of Tdap, adolescents and adults are recommended to receive a booster dose of tetanus and diphtheria toxoids (Td) vaccine every 10 years or when indicated for wound management (*4*,*5*). In 2012, in an effort to reduce the burden of pertussis in infants, ACIP recommended a dose of Tdap for women during each pregnancy (*6*).

For the purposes of this report, DTaP and Tdap are used as general terms for diphtheria toxoid, tetanus toxoid, and

Corresponding preparer: Jennifer L. Liang, National Center for Immunization and Respiratory Diseases, CDC. E-mail: JLiang@cdc.gov.

acellular pertussis vaccines, and DT and Td are used for diphtheria and tetanus toxoid–containing vaccines. Any of the vaccine formulations licensed in the United States can be used in an age-appropriate manner to implement these vaccination recommendations. Both DTP and monovalent tetanus toxoid (TT) vaccines are discussed for historical purposes and no longer are manufactured or available in the United States.

ACIP recommendations for vaccination for pertussis, tetanus, and diphtheria and guidance for use are described elsewhere in this report (see Recommendations for Use of Pertussis, Tetanus, and Diphtheria Vaccines) (Table 1). Details regarding contraindications, precautions, and special circumstances are described elsewhere in this report (see Recommendations for Use of Pertussis, Tetanus, and Diphtheria Vaccines) (Tables 2 and 3). In 2013, after review of available data, ACIP did not support a universal recommendation for a second dose of Tdap for the general population (see No Additional Doses of Tdap For the General Population). In 2014 and 2015, ACIP did not support a second dose of Tdap for health care personnel or close contacts of infants.

TABLE 1. Recommended pertussis, diphtheria, and tetanus vaccination schedule — Advisory Committee on Immunization Practices, 2017

Vaccine	Age group/Indication	Recommended schedule
DTaP*	2 mos–6 yrs	Primary (3 doses) • 1 dose at ages 2, 4, and 6 mos 1st booster • 1 dose at age 15–18 mos 2nd booster • 1 dose at age 4–6 yrs
Tdap†	7–10 yrs§	Not routinely recommended; refer to "Persons with incomplete or unknown vaccine history"
	11–18 yrs	11–12 yrs, 1 dose 13–18 yrs, 1 dose if not vaccinated previously with Tdap
	≥19 yrs	1 dose if not vaccinated previously with Tdap
	Pregnant women¶	1 dose each pregnancy; preferred at 27–36 wks' gestation
Td†		Booster • 1 dose every 10 yrs

Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Td = tetanus and diphtheria toxoids vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.
* See Table 4 for vaccine type and ages for licensed use.
† See Table 5 for vaccine type and ages for licensed use.
§ Off-label use of Tdap in persons aged 7–9 years.
¶ Off-label use of Tdap.

Methods

Periodically, ACIP reviews available information to inform the development or revision of its vaccine recommendations. In February 2009, the ACIP Pertussis Vaccines Work Group was formed to review and revise previously published vaccine recommendations for DTaP, DT, Td, TT, and Tdap because of 1) the availability of new licensed DTaP vaccine products since 1997; 2) multiple ACIP updates to the adolescent and adult Tdap recommendations; 3) new U.S. Food and Drug Administration (FDA) age indications for both Tdap vaccine products; 4) the need to incorporate pertussis, tetanus, and diphtheria vaccine recommendations into a single document; 5) new data on Tdap coverage, impact, and vaccine effectiveness; and 6) the discontinuation of TT vaccine manufacturing and availability in the United States. The work group held teleconference meetings monthly from April 2009 through April 2015. In addition to ACIP members, the work group included participants from the American Academy of Family Physicians (AAFP), American Academy of Pediatrics (AAP), American College of Obstetricians and Gynecologists (ACOG), the Association of Immunization Managers, CDC, the Council of State and Territorial Epidemiologists, FDA, the Infectious Diseases Society of America, the National Institute of Health, and other infectious disease experts (*7*).*

Issues reviewed and considered by the work group included epidemiology of pertussis, tetanus, and diphtheria in the United States; use of Tdap vaccine among persons aged ≥65 years, children aged 7–10 years, health care personnel, and women during pregnancy; minimum interval between the last tetanus toxoid–containing vaccine and receipt of Tdap; effectiveness of Tdap vaccine; and vaccine safety. Recommendation options were developed and discussed by the work group. The work group evaluated the available published and unpublished data and evidence regarding pertussis disease epidemiology in the United States, decision analyses, cost-effectiveness, programmatic considerations, vaccine immunogenicity, vaccine safety, and postlicensure Tdap vaccine effectiveness. When evidence was lacking, the recommendations incorporated expert opinion of the work group members (*6,8–10*).

From June 2010 through June 2015 at 11 ACIP meetings, a summary of the data reviewed, work group discussions, and proposed changes to recommendations were presented. During these 11 meetings, changes to recommendations, if made, were approved either as submitted or as amended by ACIP and then published as policy notes in *MMWR*. A summary of these recommendations is available at https://stacks.cdc.gov/view/cdc/52821. During the preparation of this summary report, nonsystematic literature searches

*A list of the members of the Work Group appears on page 43.

TABLE 2. Contraindications and precautions* for DTaP, Tdap, DT, and Td vaccines

Vaccine	Contraindications	Precautions*
DTaP	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component†,§ Encephalopathy (e.g., coma, decreased level of consciousness, or prolonged seizures) not attributable to another identifiable cause within 7 days of administration of previous dose of DTP or DTaP¶	Progressive or unstable neurologic disorder, including infantile spasms, uncontrolled seizures or progressive encephalopathy; defer DTaP until neurologic status clarified and stabilized Guillain-Barré syndrome <6 weeks after previous dose of tetanus toxoid–containing vaccine History of Arthus-type hypersensitivity reactions after a previous dose of tetanus or diphtheria toxoid–containing vaccines; defer vaccination until at least 10 years have e–lapsed since the last tetanus toxoid–containing vaccine Moderate or severe acute illness with or without fever
Tdap	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component§ Encephalopathy (e.g., coma, decreased level of consciousness, or prolonged seizures) not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP, DTaP, or Tdap**	Progressive or unstable neurological disorder, uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized; these precautions are for pertussis components Guillain-Barré syndrome <6 weeks after a previous dose of tetanus toxoid–containing vaccine History of Arthus-type hypersensitivity reactions after a previous dose of tetanus or diphtheria toxoid–containing vaccines; defer vaccination until at least 10 years have elapsed since the last tetanus toxoid–containing vaccine Moderate or severe acute illness with or without fever
DT, Td	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component§	Guillain-Barré syndrome <6 weeks after previous dose of tetanus toxoid–containing vaccine History of Arthus-type hypersensitivity reactions after a previous dose of tetanus or diphtheria toxoid–containing vaccines; defer vaccination until at least 10 years have elapsed since the last tetanus toxoid–containing vaccine Moderate or severe acute illness with or without fever

Abbreviations: DT = diphtheria and tetanus toxoids vaccine; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; DTP = diphtheria toxoid, tetanus toxoid and whole-cell pertussis vaccine; MenACWY = quadrivalent meningococcal conjugate, serogroups A, C, W, Y vaccine; Td = tetanus and diphtheria toxoids vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

* Events or conditions listed as precautions should be reviewed carefully. Benefits of and risks for administering a specific vaccine to a person under these circumstances should be considered. If the risk from the vaccine is believed to outweigh the benefit, the vaccine should not be administered. If the benefit of vaccination is believed to outweigh the risk, the vaccine should be administered. Whether and when to administer DTaP to children with proven or suspected underlying neurologic disorders should be decided on a case-by-case basis.

† Further vaccination with any of the three components of DTaP should be deferred because of uncertainty as to which component of the vaccine might be responsible.

§ Because of the importance of tetanus vaccination, persons who experience anaphylactic reactions should be referred to an allergist to determine whether they have a specific allergy to tetanus toxoid and can be desensitized to tetanus toxoid.

¶ In such cases, DT vaccine should be administered for the remaining doses in the vaccination schedule to ensure protection against diphtheria and tetanus.

** This contraindication is for the pertussis component, and these persons should receive Td instead of Tdap.

for specific topics were conducted in PubMed and Google Scholar for published literature in English available in print or online to provide more updated data and information since publication of any ACIP vaccine recommendations for DTaP, DT, Td, TT, and Tdap published in *MMWR*; a document containing the literature search topics, search terms, search period, and references selected is available at https://stacks.cdc.gov/view/cdc/52823. The contents of this summary report were presented to ACIP and approved at the October 2016 ACIP meeting. During the review process, CDC modified the summary to update and clarify wording. ACIP meeting minutes, including declaration of ACIP member conflicts of interest, are available at https://www.cdc.gov/ vaccines/acip/meetings/meetings-info.html. One ACIP member abstained from voting because of a conflict of interest.

Background and Epidemiology of Pertussis

Pertussis is an acute respiratory disease caused by the bacterium *Bordetella pertussis* (*11*). Classic pertussis disease is characterized by three phases of illness: catarrhal, paroxysmal, and convalescent (*11–13*). During the catarrhal phase, infected persons experience coryza (inflammation of the mucous membranes of the nasal cavities), mild occasional cough, and low-grade fever. The paroxysmal phase is characterized by spasmodic cough, posttussive vomiting, and inspiratory whoop. Symptoms slowly improve during the convalescent phase, which generally lasts 7–10 days, but can last for months. Factors that affect the clinical presentation of pertussis include age, the level of immunity, history of vaccination, and use of antimicrobials early during the course of the illness (*11*).

TABLE 3. Conditions that are not contraindications to vaccination with DTaP, DT, Td, and Tdap

Vaccine	Conditions commonly misperceived as contraindications (i.e., vaccine may be administered under these conditions)
General for DTaP, DT, Td, Tdap	Mild acute illness with or without fever Mild-to-moderate local reaction (i.e., swelling, redness, soreness); low-grade or moderate fever after previous dose Lack of previous physical examination in well-appearing person Current antimicrobial therapy Convalescent phase of illness Preterm birth Recent exposure to an infectious disease History of penicillin allergy, other nonvaccine allergies, relatives with allergies, or receiving allergen extract immunotherapy
DTaP	Fever of <105°F (<40.5°C), fussiness or mild drowsiness after a previous dose of DTP/DTaP Family history of seizures Family history of sudden infant death syndrome Family history of an adverse event after DTP or DTaP administration Stable neurologic conditions (e.g., cerebral palsy, well-controlled seizures, or developmental delay) History of collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP History of seizure with or without fever within 3 days after receiving a previous dose of DTP/DTaP History of persistent, inconsolable crying lasting >3 hours within 48 hours after receiving a previous dose of DTP/DTaP
Tdap	Fever of ≥105°F (≥40.5°C) for <48 hours after vaccination with a previous dose of DTP or DTaP History of collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP History of seizure with or without fever within 3 days after receiving a previous dose of DTP/DTaP History of persistent, inconsolable crying lasting >3 hours within 48 hours after receiving a previous dose of DTP/DTaP History of extensive limb swelling after DTP/DTaP/Td that is not an Arthus-type reaction Stable neurologic disorder History of brachial neuritis Breastfeeding Immunosuppression

Abbreviations: DT = diphtheria and tetanus toxoids vaccine; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; DTP = diphtheria toxoid, tetanus toxoid and whole-cell pertussis vaccine; Td = tetanus and diphtheria toxoids vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.
Source: Adapted from CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep-2011;60(No. RR-2).

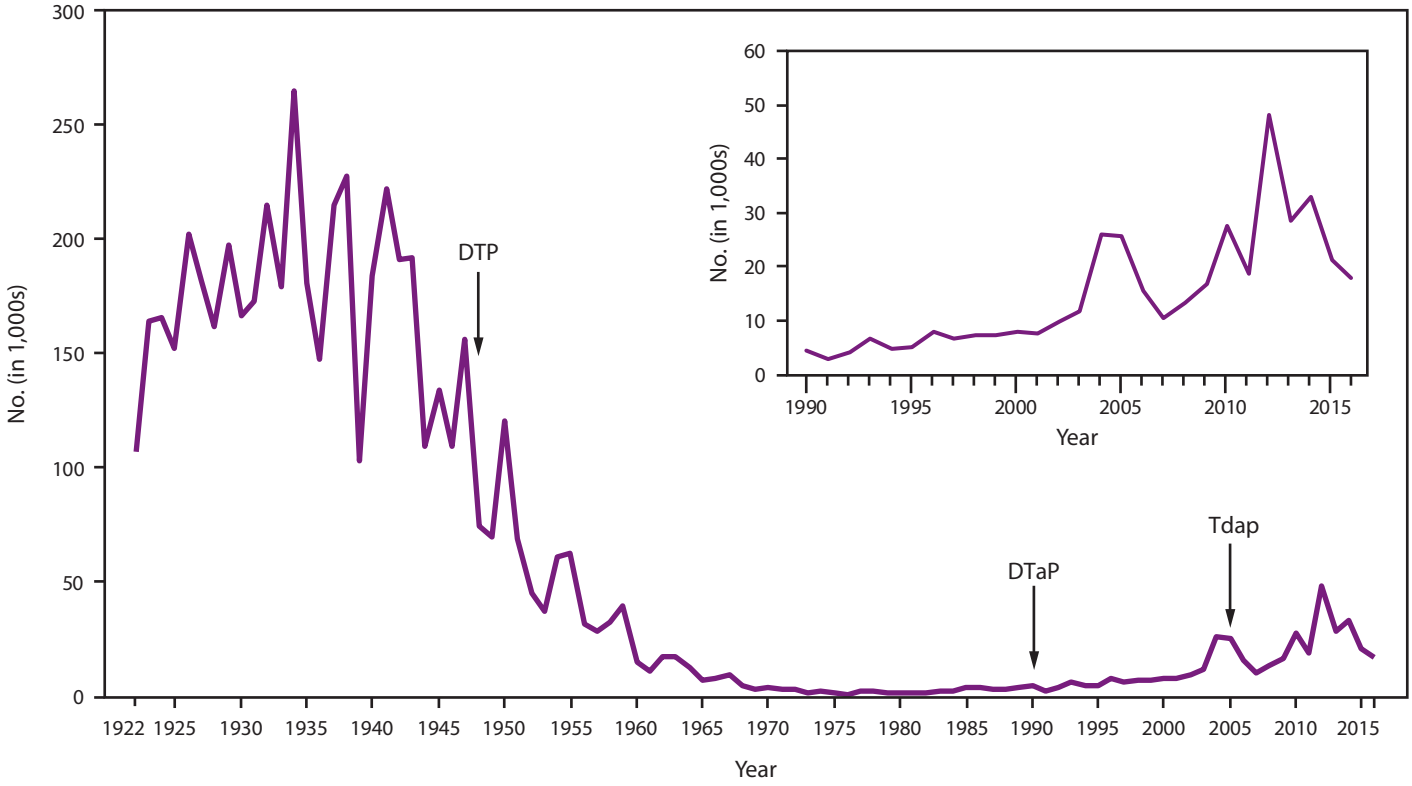
B. pertussis is transmitted primarily from person to person through aerosolized respiratory droplets generated by coughing or sneezing. Persons with pertussis are most infectious during the catarrhal and early paroxysmal phases of illness (*12*). Pertussis generally is treated with antibiotics, which are used to control the signs and symptoms and to prevent infected persons from spreading the infection to others. Recommended antibiotics for pertussis include azithromycin, clarithroymycin, erythromycin, or trimethoprim-sulfamethoxazole (TMP-SMX). Guidance for the treatment of pertussis has been published previously (*14*). Guidance on postexposure prophylaxis of pertussis is available at https://www.cdc.gov/pertussis/outbreaks/pep.html.

Epidemiology of Pertussis in the United States

In the United States, pertussis is a nationally notifiable disease (*15*). During 1934–1943, before the introduction of childhood pertussis vaccination in the United States, an annual average of 200,752 pertussis cases and 4,034 pertussis-related deaths were reported (*16*). After introduction of whole-cell pertussis vaccine during the 1940s, the number of reported pertussis cases declined dramatically, reaching an historic low of 1,010 in 1976 (Figure 1) (*3*). Since the 1980s, there has been an overall trend of an increase in reported pertussis cases, especially among adolescents and adults (*17–19*). Although pertussis is cyclic in nature, with peaks in disease every 3 to 5 years, the peaks have gotten higher, notably in 2004 (25,827 cases), 2005 (25,616 cases), 2010 (27,500 cases), and 2012 (48,277 cases) (*20–24*). The increase in reported pertussis cases is likely attributable to an actual increase in the burden of disease; however, other factors have contributed to the estimates of disease burden. These include improvements in diagnostic testing, increased health care personnel and public awareness of pertussis, and better reporting of cases (*17*,*18*,*25–27*). A growing body of evidence strongly suggests that the change in vaccines in the late 1990s from whole-cell pertussis vaccines to acellular pertussis vaccines in the childhood vaccine series has caused the age-specific increases in pertussis incidence among children aged 7–10 years observed in the mid-2000s because of waning immunity (Figure 2) (*28–30*).

In the United States, coverage with pertussis-containing vaccines varies across age groups. Vaccination coverage with DTaP in children aged 19–35 months remains consistently high, at 95.0% for ≥3 DTaP doses and 84.6% for ≥4 DTaP doses reported in 2015 (*31*). Coverage for ≥4 DTaP doses

FIGURE 1. Number of reported pertussis cases — United States, 1922–2016



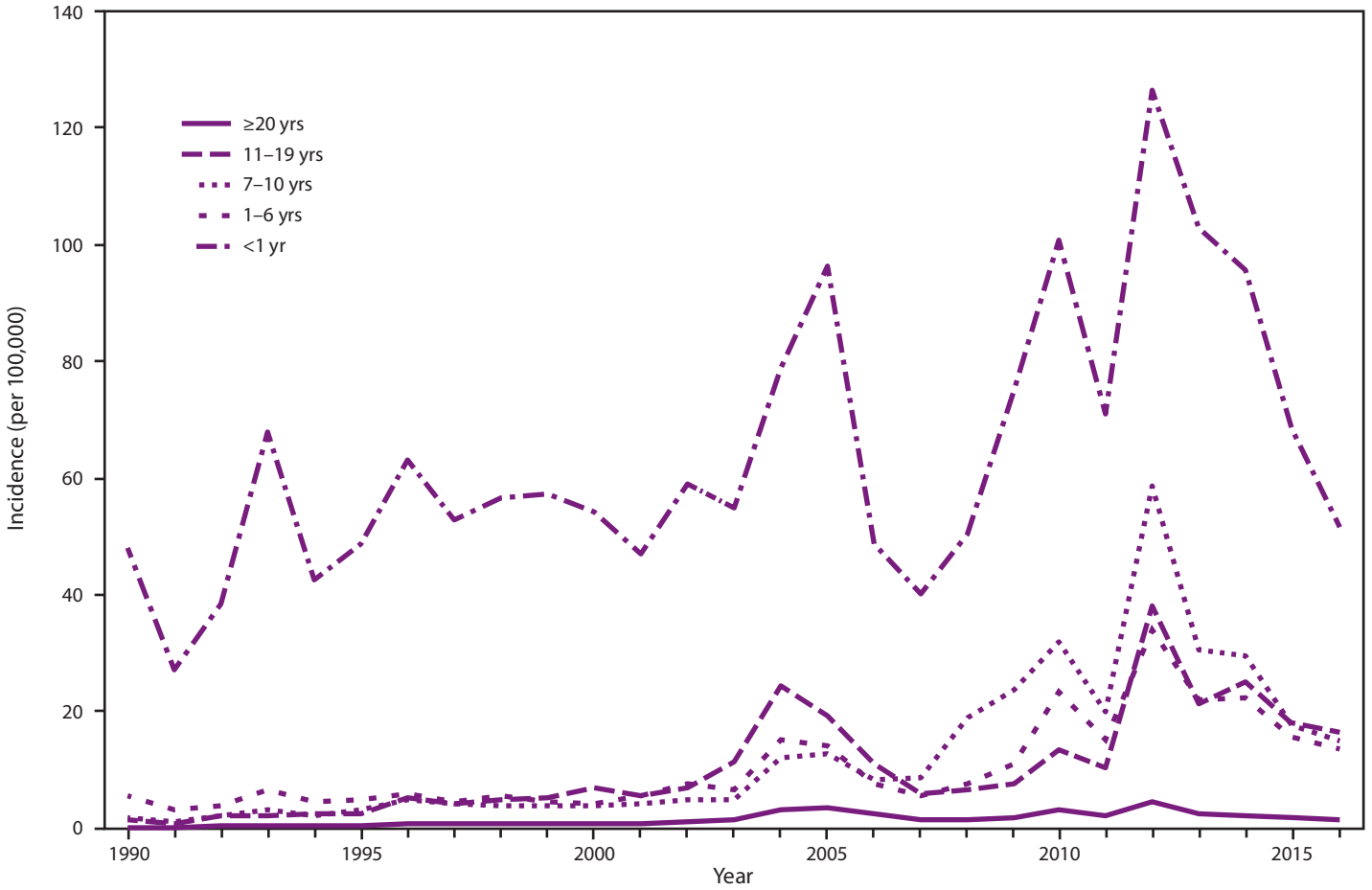
Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; DTP = diphtheria toxoid, tetanus toxoid and whole-cell pertussis vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine.
Sources: National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922–1949, passive reports to the U.S. Public Health Service.

is below the *Healthy People 2020* target of 90% (*32*). Since the introduction of Tdap in 2005, coverage with Tdap in adolescents aged 13–17 years has increased substantially, from 10.8% in 2006 to 86.4% in 2015 (*33*,*34*). Tdap coverage among adolescents has met the *Healthy People 2020* target of 80% (*35*). In 2015, for adults aged ≥19 years, the proportion receiving any tetanus toxoid–containing vaccine (e.g, TT, Td, or Tdap) during the preceding 10 years was 62.1% (19–49 years), 64.1% (50–64 years), and 56.9% (≥65 years); Tdap coverage was 23.1% (*36*). Among pregnant women, Tdap coverage during the 2015–2016 influenza season was 48.8% (*37*).

Although pertussis vaccination has resulted in a markedly reduced incidence of pertussis cases and deaths, pertussis still causes morbidity in persons of all ages. Compared with all other age groups, infants aged <12 months have substantially higher rates of pertussis disease, complications, hospitalizations, and pertussis-related deaths (*38*–*40*). The highest percentage of pertussis-related hospitalizations and deaths occurs among infants aged <2 months (CDC, unpublished data, 2016) (*38*,*41*). During 2004–2016, among all infants hospitalized for pertussis, 54.4% were aged <2 months; of the infant pertussis cases who died, 85.5% were aged <2 months and too young to have received any doses of pertussis vaccines (CDC, unpublished data, 2016). Over the past decade, with the changing pertussis epidemiology, a shift in the source of pertussis transmission to infants has been observed, with siblings rather than mothers being the most common source of pertussis infection for infants (*40*,*42*,*43*).

Although infants have substantially higher rates of reported pertussis compared with other age groups, an increase in the number of reported pertussis cases among children and adolescents since the mid-2000s has been attributed to the waning of acellular pertussis vaccine-induced immunity (Figure 2). This increase was first observed in children aged 7–10 years who were among the first birth cohorts to exclusively receive 5 doses of acellular pertussis (DTaP) vaccine following the switch from DTP in 1997 (*28*). As this birth cohort aged, an increase in reported pertussis cases also was observed among those aged 13–14 years in 2012 (*29*,*44*). Continued monitoring of national surveillance data will permit further characterization of the impact of acellular pertussis vaccines on the evolving epidemiology of pertussis that has been observed over the past decade.

FIGURE 2. Annual incidence* of pertussis, by age group — United States, 1990–2016



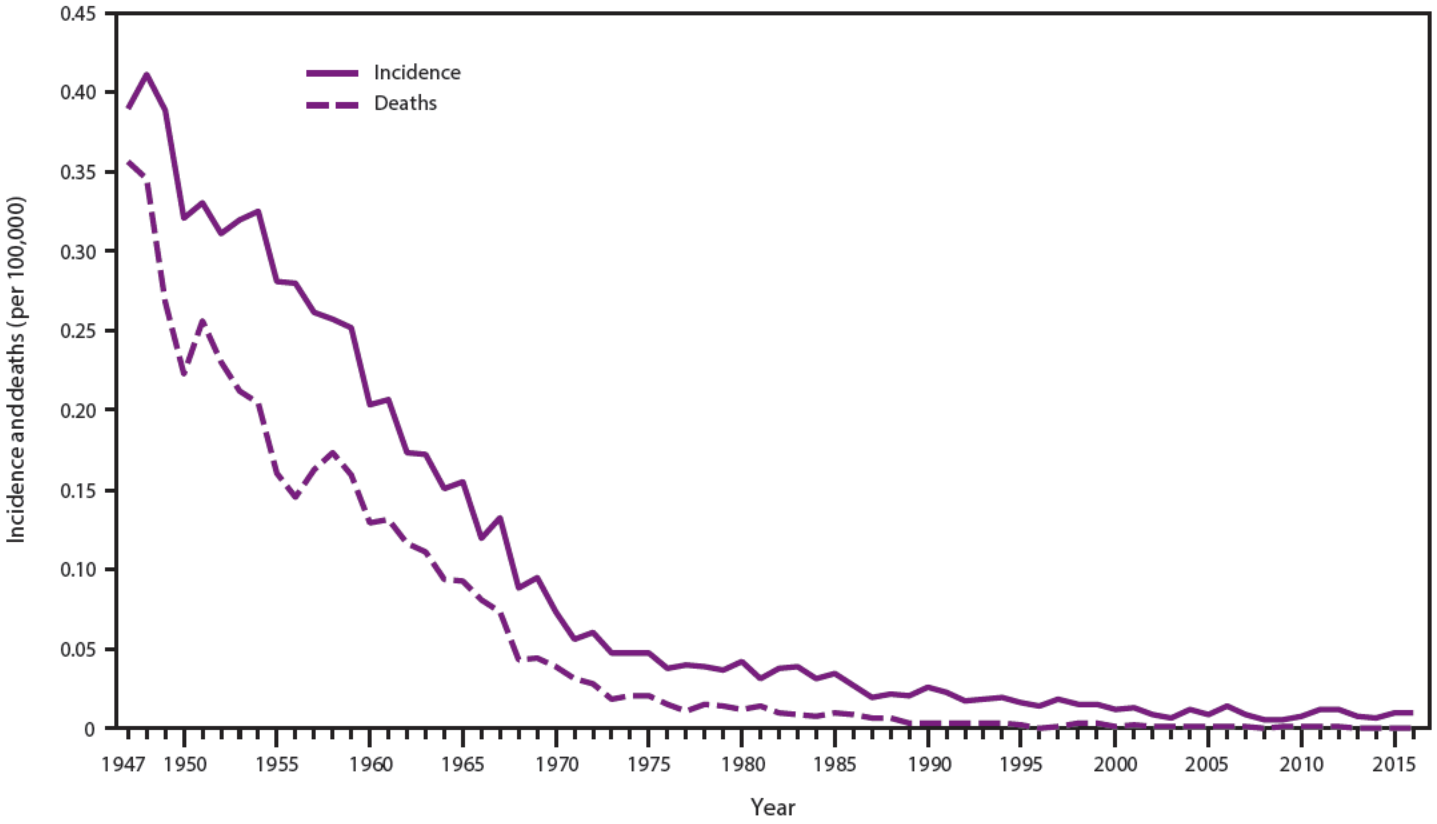
Sources: National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System.
* Per 100,000 population.

Background and Epidemiology of Tetanus

Tetanus is a life-threatening but vaccine-preventable disease caused by a potent neurotoxin produced by *Clostridium tetani*. The organism is a ubiquitous, spore-forming, motile Gram-positive bacillus found in high concentrations in soil and animal excrement. *C. tetani* spores enter the body through breaches in the skin or mucous membranes. Germination of *C. tetani* spores occurs under anaerobic conditions, such as in necrotic tissue that can result from deep puncture wounds or blunt trauma. *C. tetani* bacilli vegetate and produce tetanospasmin, a powerful exotoxin that binds irreversibly with neural tissue and causes spasms and rigidity of skeletal muscles. Direct person-to-person transmission of *C. tetani* does not occur (*45*).

The incubation period from injury to symptom onset varies from 3 to 21 days (median: 7 days), with extremes of 1 day to several months. The incubation period depends on the severity and site of the wound. Shorter incubation periods are associated with more severe disease and a poorer prognosis; longer incubation periods are associated with injuries furthest from the central nervous system. The course of disease is variable but is usually intense for ≥4 weeks before subsiding. The convalescent period is usually protracted and long-term neurologic sequelae and intellectual and behavioral abnormalities might follow recovery. The case-fatality ratio for tetanus is highest in infants and the elderly, and can be as high as 100% without high-quality medical care, but is approximately 10%–20% even in modern health care facilities (*46*).

FIGURE 3. Annual incidence* of and deaths attributable to tetanus — United States, 1947–2016



Sources: National Notifiable Diseases Surveillance System and passive reports to the U.S. Public Health Service.
* Per 100,000 population.

Epidemiology of Tetanus in the United States

Tetanus is a nationally notifiable disease in the United States (*15*). After the introduction of universal vaccination with tetanus toxoid–containing (TT) vaccines in the mid-1940s, the incidence of reported tetanus in the United States declined by >98%, from 0.39 per 100,000 population in 1947, when national reporting began, to 0.01 per 100,000 population by 2016 (CDC, unpublished data, 2016) (Figure 3). The decline in incidence occurred across all age groups. Deaths from tetanus also declined similarly during this period. The decline in morbidity and mortality is attributable to widespread use of tetanus toxoid–containing vaccines; improved wound management, including use of tetanus prophylaxis in emergency departments; improved hygiene during childbirth; increased levels of maternal immunity; and expanded urbanization (*45*).

Tetanus occurs primarily among older adults (*47*). During 2001–2016, three neonatal tetanus cases and 459 non-neonatal tetanus cases were reported to the National Notifiable Diseases Surveillance System (NNDSS). The median age for non-neonatal cases was 44.0 years (range: 2–95 years); 60% of cases occurred in males (CDC, unpublished data, 2016). The risk for both tetanus disease and mortality was higher among persons aged ≥65 years than among persons aged <65 years (*48*). Tetanus occurs almost exclusively among persons who are unvaccinated or inadequately vaccinated or in those whose vaccination histories are unknown or uncertain. The case-fatality ratio for reported tetanus in the United States declined from 18% (1998–2000) to 8.0% (2001–2016) (CDC, unpublished data, 2016) (*48*,*49*).

Population Immunity

The minimum level of circulating antitetanus antibodies associated with protection against tetanus is assay-specific. The acceptable level of circulating antitetanus antibodies required for protection is 0.01 IU/mL as measured in an in vivo toxin neutralization assay. When in vitro methods, such as standard enzyme-linked immunosorbent assays (ELISA), are used, antibody level readings of at least 0.1–0.2 IU/mL are considered protective (*50*).

The National Health and Nutritional Examination Survey (NHANES III), a population-based national serosurvey

conducted in the United States during 1988–1994, found that approximately 80% of adolescents aged 12–19 years and >80% of adults aged 20–39 years had seroprotective concentrations of antitetanus toxoid antibodies (*51*). In this survey, a standard ELISA test was used to assess antibody levels with levels >0.15 IU/mL considered as protective. The proportions of persons lacking protective levels of circulating antibodies against tetanus toxin increased with age, with a greater rate of decline among women. By age 70 years, only 45% of men and 21% of women had a protective level of antibodies to tetanus. Previous military service was associated with a higher prevalence of protective antibodies to tetanus in men, presumably because of routine vaccination during military service. The low prevalence of detectable antibodies and the high proportion of tetanus cases among older adults reflects the high proportion of older adults who possibly never received primary DTP vaccination or have waning immunity if they never received subsequent tetanus toxoid–containing booster doses (*48*,*51*).

Prevention

Immunity to tetanus toxin is rarely if ever acquired naturally, but tetanus is preventable through the use of highly effective tetanus toxoid–containing vaccines (i.e., DTaP, DT, Td, or Tdap) (*50*). Completing a 5-dose childhood vaccination series with DTaP before age 7 years is necessary for developing protective levels of antitetanus antibodies that persist into the adolescent years, when a booster dose of vaccine is needed; thereafter, decennial boosters with Td administered throughout adulthood are recommended to maintain protection against tetanus (*52*).

Background and Epidemiology of Diphtheria

Respiratory diphtheria is an acute, communicable infectious illness caused by toxigenic strains of *Corynebacterium diphtheriae*, which are nonmotile, nonencapsulated, club-shaped, Gram-positive bacilli. Although rare, toxin-producing *Corynebacterium ulcerans* can also cause a diphtheria-like illness (*53*). Vaccination with diphtheria toxoid-containing vaccines (i.e., DTaP, DT, Tdap, or Td) prevents diphtheria (*54*). Toxin-producing strains of *C. diphtheriae* can cause disease in susceptible persons by multiplying and producing diphtheria toxin in either nasopharyngeal or skin lesions. The classic feature of respiratory diphtheria is a gray-colored pseudomembrane that is firmly adherent to the mucosa lining the nasopharynx, tonsils, or larynx. The extension of the pseudomembrane into the trachea-bronchial tree might cause life-threatening airway obstruction. In addition, systemic absorption and dissemination of diphtheria toxin can cause toxin-mediated cardiac and neurologic complications (*55*).

Epidemiology of Diphtheria in the United States

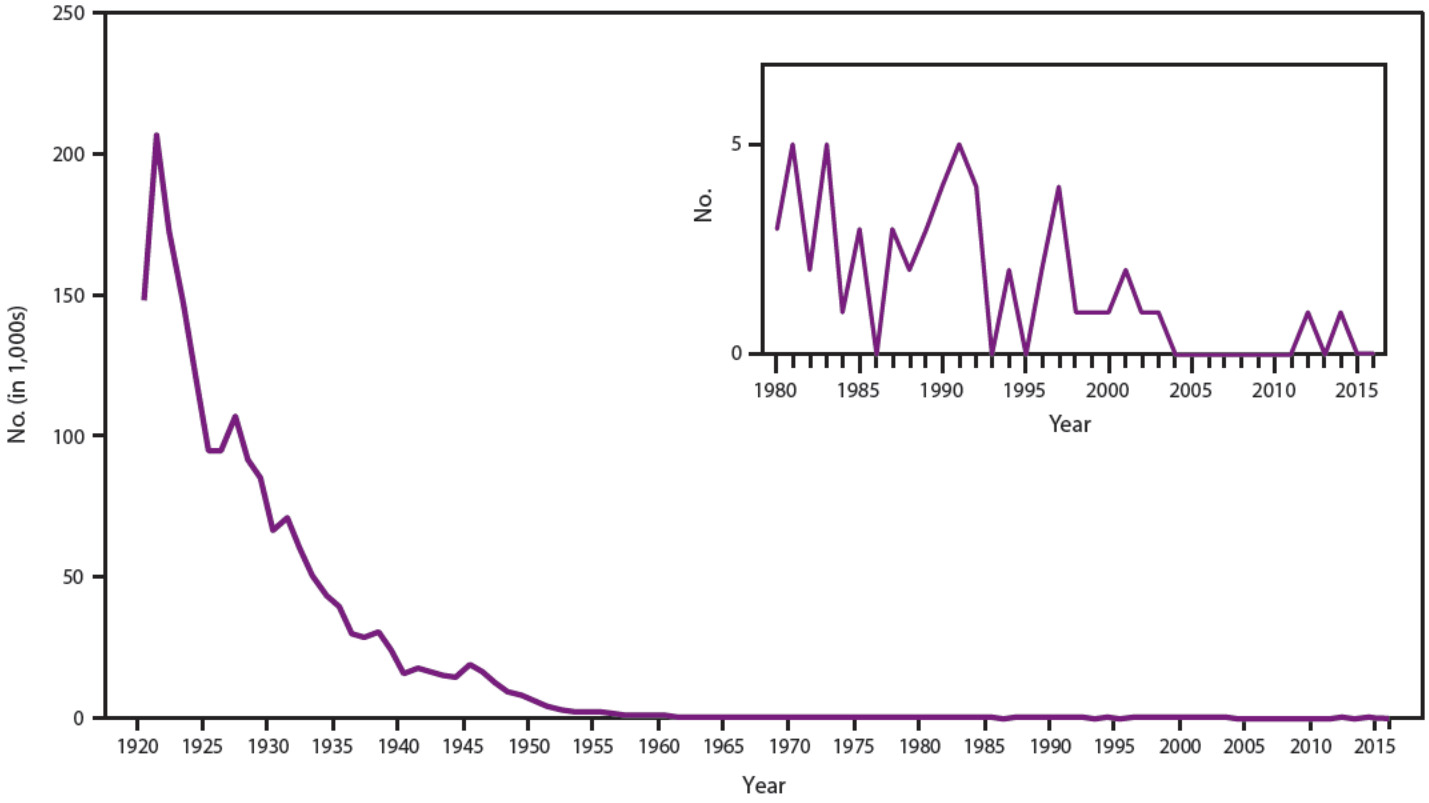
In the United States, diphtheria is a nationally notifiable disease (*15*). Reported diphtheria cases from all anatomical sites declined from approximately 200,000 in 1921 to 15,536 in 1940 (Figure 4). This decline continued after the introduction of universal childhood vaccination in the late 1940s and, in 1980, only two cases of diphtheria were reported (*56*). Since 1980, cutaneous diphtheria has not been reportable and only respiratory cases are reportable to NNDSS. During 1996–2016, a total of 13 cases were reported (CDC, unpublished data, 2016) (*21–23*,*57–63*). Although no cases were reported during 2004–2011, a probable case with a positive polymerase chain reaction (PCR) test for the diphtheria toxin gene ("tox") occurred in 2012, and a case positive by culture with nontoxigenic *C. diphtheriae* was reported in 2014 (*24*,*47*).

Although childhood DTaP vaccination coverage is >80% in the United States, immunity acquired from childhood vaccination wanes in the absence of decennial boosters, and older adults might not be adequately protected (*51*). An analysis of NHANES III indicated that only 60% of the overall population sample had immunity to diphtheria (defined as an antidiphtheria toxoid concentration of >0.1 IU/mL). This immunity declined progressively with increasing age from 91% at age 6–11 years and 80% among adolescents aged 12–19 years, to approximately 30% among those aged 60–69 years (*54*). Data from the 2015 National Immunization Survey (NIS) indicated that 61.6% of adults aged 19–49 years received any tetanus toxoid–containing vaccination during the preceding 10 years, 64.1% (aged 50–64 years), and 56.9% (aged ≥65 years) (*36*).

Although rare in the United States, exposure to diphtheria remains possible during travel to countries with endemic disease[†] or from imported cases (*64*). Information about the clinical management of diphtheria, including use of diphtheria antitoxin, and the public health response is available at https://www.cdc.gov/diphtheria/clinicians.html.

[†] Information available at http://wwwnc.cdc.gov/travel/page/yellowbook-home.

FIGURE 4. Number of reported diphtheria cases — United States, 1920–2016



Sources: National Notifiable Diseases Surveillance System and passive reports to the U.S. Public Health Service.

Vaccines for Prevention of Pertussis, Tetanus, and Diphtheria

Vaccines of different compositions, formulations, and combinations are licensed and available in the United States for different age groups to prevent pertussis, tetanus, and diphtheria (Tables 4 and 5). The indication and age for vaccination might differ by vaccine product and licensure. In certain situations, the off-label use of Tdap vaccine has been recommended, including the absence of a minimum interval between the last tetanus toxoid–containing vaccine and receipt of Tdap, catch-up vaccination for those aged 7–10 years, and vaccination of women during each pregnancy (*6*,*8*).

Tetanus Component

TT vaccine became commercially available in the United States in 1938. After the 1940s, tetanus toxoid was available in combination with diphtheria toxoid with or without whole-cell pertussis antigens in vaccines. Although single antigen TT was used predominantly before 1960, use of Td has replaced TT; production of TT was discontinued in 2013.

In the United States, manufactured tetanus toxoid is adsorbed to aluminum salt adjuvants (aluminum hydroxide, aluminum phosphate, or aluminum sulfate), thimerosal-free, and highly purified, with <0.02% formaldehyde and <1.25 mg aluminum. Pediatric formulations of tetanus toxoid–containing vaccines (DT and DTaP) contain 5–10 limit of flocculation (Lf) units of the antigen (Table 4). Adolescent and adult formulations (Td and Tdap) contain ≤5 Lf units of tetanus toxoid per 0.5 ml dose (Table 5). More than a single dose of vaccine is required to induce immunologic protection, and booster doses are required to maintain protection.

Immunogenicity and Effectiveness

Although no randomized controlled clinical trial of the efficacy of tetanus toxoid in preventing disease ever has been conducted, evidence from observational studies consistently supports the effectiveness of vaccination. The incidence of tetanus among U.S. army personnel declined from 13.4 per 100,000 during World War I (when personnel were unvaccinated) to 0.44 per 100,000 during World War II (when personnel routinely were vaccinated with TT and also vaccinated following an injury) (*65*). Similar observations were made among British army personnel during the same periods during the two world wars

TABLE 4. Composition of vaccines containing tetanus toxoid, diphtheria toxoid, and acellular pertussis antigens and age for approved use by vaccine type for persons aged less than 7 years — United States, 2017

Vaccine type	Trade name	Manufacturer	Pertussis antigens (μg)				Diphtheria toxoid (Lf)	Tetanus toxoid (Lf)	Age for approved use in routine and catch-up immunization schedules				
			PT	FHA	PRN	FIM			2 mos	4 mos	6 mos	15–18 mos	4–6 yrs
DTaP vaccines*													
DTaP	Infanrix	GlaxoSmithKline	25	25	8		25	10	X†	X	X	X	X
DTaP	Daptacel	Sanofi Pasteur, Inc.	10	5	3	5	15	5	X†	X	X	X	X
Combination vaccines with DTaP*													
DTaP-IPV-HepB	Pediarix	GlaxoSmithKline	25	25	8		25	10	X†	X	X	X	X§
DTaP-IPV-Hib	Pentacel	Sanofi Pasteur, Inc.	20	20	3	5	15	5	X†	X	X	X	X¶
DTaP-IPV	Kinrix	GlaxoSmithKline	25	25	8		25	10					X
DTaP-IPV	Quadracel	Sanofi Pasteur, Inc.	20	20	3	5	15	5					X
DT vaccine*													
DT	No trade name	Sanofi Pasteur, Inc.					6.7	5	X†	X	X	X	X

Abbreviations: DT= diphtheria and tetanus toxoids vaccine; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; FDA= U.S. Food and Drug Administration; FHA = filamentous hemagglutinin; FIM = fimbriae types 2 and 3; HepB = hepatitis B; Hib = *Haemophilus influenza* type b; IPV = inactivated poliovirus; Lf = limit of flocculation unit; PRN = pertactin; PT = pertussis toxin.
* Vaccine dosage and administration: 0.5mL intramuscular injection.
† FDA-approved for use in infants as young as 6 weeks.
§ FDA-approved for use through age 6 years (prior to 7th birthday).
¶ FDA-approved for use through age 4 years (prior to 5th birthday).

TABLE 5. Composition of vaccines containing tetanus toxoid, diphtheria toxoid, and acellular pertussis antigens and age for approved use by vaccine type for persons aged ≥7 years — United States, 2017

Vaccine type	Trade name	Manufacturer	Age (yrs) for approved use in routine and catch-up immunization schedules	Pertussis antigens (μg)				Diphtheria toxoid (Lf)	Tetanus toxoid (Lf)
				PT	FHA	PRN	FIM		
Tdap vaccines*									
Tdap	Adacel	Sanofi Pasteur, Inc.	10–64	2.5	5	3	5	2	5
Tdap	Boostrix	GlaxoSmithKline	≥10	8	8	2.5		2.5	5
Td vaccines*									
Td	No trade name	MassBiologics	≥7					2	2
Td	Tenivac	Sanofi Pasteur, Inc.	≥7					2	5

Abbreviations: FHA = filamentous hemagglutinin; FIM = fimbriae types 2 and 3; Lf = limit of flocculation unit; PRN = pertactin; PT = pertussis toxin; Td = tetanus and diphtheria toxoids vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid vaccine, and acellular pertussis vaccine.
* Vaccine dosage and administration: 0.5mL intramuscular injection.

(*66*). The effectiveness of tetanus toxoid is very high, although not 100%. Although data on a minimum antitetanus antibody cut-off level for protection are sparse, it is generally accepted that levels at 0.01 IU/mL and above by in vivo toxin neutralization assay are protective (*46*,*54*). One dose of tetanus toxoid vaccine provides little, if any, immunity. After receiving 3 doses of tetanus toxoid–containing vaccine, virtually all infants and adults develop protective tetanus antitoxin titers >0.1 IU/mL. A primary immunization series with 3 doses of tetanus toxoid induced a mean antitetanus level of 0.2 IU/mL, and antibody levels from primary vaccination provide protection from tetanus for approximately 3–5 years (*67*–*69*). Additional booster tetanus doses heighten the immune response and prolong the duration of protective immunity. Booster doses at age 4–8 years and during adolescence provide long-lasting protective immunity and a duration of 20–30 years from the last dose has been suggested (*50*).

Diphtheria Component

Diphtheria toxoid was shown to be immunogenic in 1923 and has since been used as the immunizing agent against diphtheria (*70*). The immunogenicity of diphtheria toxoid is improved when it is adsorbed onto an adjuvant (most commonly aluminum hydroxide or aluminum phosphate). By the mid-1940s, diphtheria toxoid was combined with tetanus toxoid and pertussis vaccine as DTP and later adsorbed onto an aluminum salt and used in the routine childhood vaccination program. Only vaccines containing formaldehyde-inactivated diphtheria toxin adsorbed to an aluminum salt adjuvant combined with tetanus toxoid with or without acellular pertussis vaccines are available in the United States (Tables 4 and 5). More than a single dose of vaccine is required to induce immunologic protection, and booster doses are required to maintain protection (*71*).

Immunogenicity and Effectiveness

Although no randomized controlled clinical trial of the efficacy of diphtheria toxoid in preventing disease has ever been conducted, strong evidence from observational studies supports the effectiveness of vaccination (*72*). The effectiveness of diphtheria toxoid is high, although not 100%. After receiving 3 doses of diphtheria toxoid–containing vaccines, virtually all infants develop diphtheria antitoxin titers >0.01 IU/mL (*71*,*73*,*74*). Although some DTaP products produce lower geometric mean titers than those observed after vaccination with DTP, these differences are not thought likely to be clinically significant. For primary vaccination of adults aged ≥19 years, data suggest that virtually all adults develop diphtheria antitoxin titers >0.01 IU/mL after receiving 3 doses of diphtheria toxoid–containing vaccines (*75*,*76*). A diphtheria antitoxin level of 0.01 to 0.09 IU/mL provides some degree of protection, whereas levels ≥0.1 IU/mL are considered protective and levels >1.0 IU/mL are associated with long-lasting protection (*77*). Although no level of circulating diphtheria antitoxin confers absolute protection, most reports indicate that *C. diphtheriae* infection in previously vaccinated persons is milder and less likely to be fatal (*56*,*78*,*79*). The failure of the vaccine to protect all persons exposed to *C. diphtheriae* highlights the importance of maintaining high vaccination coverage and herd immunity to prevent or limit transmission and outbreaks, as evidenced by the disappearance of diphtheria cases in industrialized countries with established vaccination programs.

Although various schedules used worldwide for primary vaccination (3 doses during infancy or 4 doses by age 15 months) appear to provide adequate protection from diphtheria in the early years of life, a booster dose is needed at age 4–6 years to maintain protection throughout the school-age years (*71*). The massive epidemic in the former Union of Soviet Socialist Republics in the 1990s strongly suggests that sustaining high vaccination coverage with a primary series of diphtheria toxoid–containing vaccine among infants and administering booster doses at school entry and throughout life are important for maintaining population immunity (*80*). In developed countries where diphtheria is well controlled, there is little to no opportunity for exposure and natural boosting of immunity from infection after childhood. The World Health Organization (WHO) recommends that persons living in areas of low endemicity or areas where disease is not endemic should receive booster doses of combined diphtheria and tetanus toxoids approximately 10 years after completing the primary series and subsequently every 10 years throughout life (*70*).

Tetanus and Diphtheria Toxoid–containing Vaccines

As of 2016, one DT vaccine product and two Td vaccine products are licensed by FDA and available in the United States (Tables 4 and 5); production of TT vaccine was discontinued in 2013, and it is no longer available in the United States.

DT

DT product (no trade name; Sanofi Pasteur, Swiftwater, Pennsylvania) is licensed by FDA for active vaccination against diphtheria and tetanus in children up to age 7 years for whom the pertussis vaccine component is contraindicated or in situations when the health care provider decides that pertussis vaccine should not be administered. The concentration of diphtheria toxoid is higher in DT vaccine compared to Td vaccine. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142732.pdf).

Td

Tenivac (Sanofi Pasteur, Swiftwater, Pennsylvania) is licensed by FDA as a booster vaccination against tetanus and diphtheria in persons aged ≥7 years. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM152826.pdf).

Td product (no trade name; manufactured by MassBiologics, Boston, Massachusetts; distributed by Grifols, Los Angeles, California) is licensed by FDA for active vaccination for the prevention of tetanus and diphtheria in persons aged ≥7 years. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM164127.pdf).

Acellular Pertussis Components

In the United States, all vaccines available for preventing pertussis are acellular pertussis formulations combined with tetanus and diphtheria toxoids. Depending on the manufacturer, the pertussis antigens included in acellular pertussis vaccines are: pertussis toxin (PT), filamentous haemagglutinin (FHA), pertactin (PRN) and/or fimbriae types 2 and 3 (FIM). The amount of pertussis antigens present differs depending on the vaccine type and manufacturer (Tables 4 and 5). No "pertussis-only" vaccines are licensed in the United States.

Interpretation of Immunogenicity Data

Vaccine efficacy studies have demonstrated a correlation between the presence of antipertussis antibodies and protection against pertussis disease, but there are no well-accepted definitive serologic or laboratory correlates of protection against pertussis (*81*–*85*). Antibody studies are useful for comparing the immune responses elicited by a single vaccine under different conditions or in different studies, whereas efficacy studies are important to measure clinical protection conferred by each pertussis vaccine (*54*).

Licensure of new pertussis vaccines is based on the overall safety profile and the demonstration of immunogenicity not inferior to U.S.-licensed pediatric DTaP products in clinical trials (*86*). In a noninferiority trial, immunogenicity, efficacy, or safety endpoints are demonstrated when a new product is at least as good as a comparator on the basis of a predefined and narrow margin for a clinically acceptable difference between the study groups (*87*).

DTaP Vaccines

DTaP vaccines consist of pertussis antigens and diphtheria and tetanus toxoids (Table 4). Depending on vaccine type and manufacturer, the composition and amount of pertussis antigen and amount of diphtheria and tetanus toxoids differs. The FDA-approved age indication for use of DTaP vaccines differs, depending upon the specific DTaP product (Table 4). Data on immunogenicity and safety of DTaP vaccines have been published (*3*,*88*–*94*).

Licensed and Available DTaP Vaccines

As of 2016, two DTaP vaccines are licensed by FDA and available in the United States: Infanrix (GlaxoSmithKline [GSK], Rixensart, Belgium) and Daptacel (Sanofi Pasteur, Swiftwater, Pennsylvania). Immunogenicity and safety data for each of these vaccines have been published (*3*,*88*,*89*,*91*).

Infanrix (GSK) is licensed by FDA for active vaccination against diphtheria, tetanus, and pertussis as a 5-dose series in infants and children aged 6 weeks through 6 years. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM124514.pdf).

Daptacel (Sanofi Pasteur) is licensed by FDA for active vaccination against diphtheria, tetanus, and pertussis as a 5-dose series in infants and children aged 6 weeks through 6 years. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM103037.pdf).

Licensed and Available Combination Vaccines That Include DTaP

As of 2016, four combination vaccines that contain the components of DTaP vaccines are licensed by FDA and available in the United States: DTaP-IPV-HepB (Pediarix, GSK, Rixensart, Belgium), DTaP-IPV (Kinrix, GSK, Rixensart, Belgium), DTaP-IPV/Hib (Pentacel, Sanofi Pasteur, Swiftwater, Pennsylvania), and DTaP-IPV (Quadracel, Sanofi Pasteur, Swiftwater, Pennsylvania). Combination vaccines with DTaP have been shown to be both safe and immunogenic, and have similar safety profiles and antibody responses compared with DTaP administered by itself (*95*–*97*).

DTaP-IPV-HepB (Pediarix) contains DTaP, inactivated poliovirus (IPV), and Hepatitis B (recombinant) (HepB). Pediarix is approved by FDA for use as a 3-dose series in infants born to hepatitis B surface antigen (HBsAg)-negative mothers. Pediarix can be administered as early as age 6 weeks through 6 years. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM241874.pdf).

DTaP-IPV (Kinrix) contains DTaP and IPV. Kinrix is licensed by FDA for use as the fifth dose of the DTaP vaccine series and the fourth dose of the IPV series in children aged 4–6 years whose previous DTaP vaccine doses were DTaP (Infanrix, GSK) and/or DTaP-HepB-IPV (Pediarix, GSK) for the first 3 doses and DTaP (Infanrix) for the fourth dose. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM241453.pdf).

DTaP-IPV/Hib (Pentacel) contains DTaP, IPV, and *Haemophilus influenzae* type b (Hib) conjugate. Pentacel is licensed by FDA for use as a 4-dose series in children aged 6 weeks through 4 years. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM109810.pdf).

DTaP-IPV (Quadracel) contains DTaP and IPV. Quadracel is licensed by FDA for use as the fifth dose of the DTaP vaccine series and the fourth or fifth dose of the IPV series in children aged 4 through 6 years who have previously received 4 doses of Pentacel and/or Daptacel vaccine. Further information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM439903.pdf).

DTaP Vaccine Immunogenicity, Efficacy, and Effectiveness

Immunogenicity of DTaP Vaccines

Infanrix (GSK): One month after receiving 3 doses of Infanrix at ages 2, 4, and 6 months, ≥83% of children had a fourfold or greater antibody response to PT, FHA, and PRN (*98*). All children developed diphtheria antitoxin titers of ≥0.1 IU/mL and tetanus antitoxin titers of ≥0.01 IU/mL (i.e., indications of immunity against these diseases) (*3*). Whether the first 3 doses were Infanrix or DTP, >80% of children aged 15–20 months had a fourfold or greater rise in serum antibody to each of the pertussis vaccine antigens after a fourth dose of Infanrix (*99*). Immunogenicity data on the fifth dose were not required for FDA approval (*100*).

Daptacel (Sanofi Pasteur): After 4 doses of Daptacel, the antibody response to pertussis antigens among U.S. infants was similar to that achieved among Swedish infants in whom efficacy was demonstrated after receiving 3 doses of Daptacel (*88*,*101*). Diphtheria antitoxin levels of ≥1.0 IU/mL were achieved by 98.5% of children, and 100% of children achieved tetanus antitoxin levels of ≥1.0 IU/mL (*101*). Licensure for use of Daptacel as a fifth dose at age 4–6 years was based on the assumption that children previously primed with this vaccine will have a robust immune response to a booster dose of the same vaccine. For diphtheria and tetanus, it was expected that most children will have protective levels of antibody following booster vaccination (*102*).

Immunogenicity of Combination Vaccines with DTaP

Pediarix (GSK) (DTaP-HepB-IPV): The immunologic response of all antigens in Pediarix (diphtheria and tetanus toxoids; pertussis antigens; Hepatitis B virus; and inactivated poliovirus Types 1, 2, and 3) following 3 doses at age 2, 4, and 6 months was generally similar to those following 3 doses of separately administered Infanrix [DTaP (GSK)], ENGERIX-B (HepB), and oral poliovirus vaccine (*89*).

Kinrix (GSK) (DTaP-IPV): The immunogenicity of all antigens in Kinrix (diphtheria and tetanus toxoids; pertussis antigens; and inactivated poliovirus Types 1, 2, and 3) was similar between groups (DTaP-IPV and separately administered DTaP and IPV vaccines) with or without a co-administered second dose of measles, mumps, and rubella (MMR) vaccine (*92*).

Pentacel (Sanofi Pasteur) (DTaP-IPV/Hib): The immunologic response of all antigens in Pentacel (diphtheria and tetanus toxoids; pertussis antigens; inactivated poliovirus types 1, 2, and 3; and *Haemophilus influenzae* Type b conjugate) following 3 or 4 doses generally was similar to those following separately administered component vaccines (*86*,*103*). Immune responses following the first and second doses were not measured (*93*).

Quadracel (Sanofi Pasteur) (DTaP-IPV): The immunogenicity of all antigens in Quadracel (diphtheria and tetanus toxoids; pertussis antigens; and inactivated poliovirus types 1, 2, and 3) was noninferior between groups (DTaP-IPV and separately administered DTaP [Daptacel] and IPV [IPOL, Sanofi Pasteur] vaccines) with or without a co-administered second dose of MMR and varicella vaccines (*94*).

Pertussis Vaccine Efficacy

The efficacy of both DTaP vaccine products (Infanrix [GSK] and Daptacel [Sanofi Pasteur]) was evaluated in prelicensure trials in which participants received a 3-dose series at ages 2, 4, and 6 months (*104*–*106*). The vaccine efficacy estimates for 3 doses of DTaP against pertussis disease[§] ranged from 79% to 89%, with a follow-up time up to 2 years after receipt of the third dose (*104*–*106*).

Postlicensure Pertussis Vaccine Effectiveness

Assessment of the 5-dose DTaP series indicated that the estimated overall effectiveness of the pertussis vaccine was 88.7% (95% confidence interval [CI] = 79.4%–93.8%); within the first year after the fifth DTaP dose, vaccine effectiveness was 98.1% (95% CI = 96.1%–99.1%) (*28*). However, vaccine effectiveness declined with increasing time since receipt of the fifth DTaP dose; by ≥5 years since the fifth DTaP dose, vaccine effectiveness was estimated at 71.2% (95% CI = 45.8%–84.8%) (*28*). Other studies support the findings of a progressive decrease in DTaP vaccine effectiveness and increased risk for pertussis over time after receipt of the fifth dose (*107*,*108*). In contrast, an early assessment of DTaP indicated 100% vaccine effectiveness against pertussis for a limited period of time after receipt of 5 doses in children up to age 5 years, but this assessment was done shortly after ACIP issued the 5-dose DTaP recommendation and the majority of participants had received DTP as the first 3 doses (*109*).

Postlicensure Safety Surveillance of DTaP

Studies conducted since the introduction of acellular pertussis vaccines in the United States have supported the safety of DTaP (*110*–*123*). A summary of these studies is available at https://stacks.cdc.gov/view/cdc/52822. Many of these studies were performed through surveillance for adverse events

[§] The case definition was a confirmed case of pertussis with ≥21 days of paroxysmal cough illness with culture or serologic confirmation of infection with *B. pertussis*.

following vaccine receipt through two systems in the United States, Vaccine Adverse Event Reporting System (VAERS) and Vaccine Safety Datalink (VSD). VAERS is a national passive surveillance system operated jointly by CDC and FDA that receives reports of adverse events following vaccination from health care personnel, manufacturers, vaccine recipients, and others (*124*). VSD is a collaborative effort of CDC and eight managed care organizations in the United States and allows for planned vaccination safety studies and timely investigation of hypotheses that arise from the review of the medical literature, reports to VAERS, changes in the vaccination schedule, or the introduction of new vaccines (*125*).

Safety of Licensed and Available DTaP Vaccines in VAERS

During January 1, 1990–July 31, 2015, VAERS received 46,448 reports involving receipt of one of the five DTaP vaccines that are available in the United States during that period (Daptacel, Infanrix, Kinrix, Pediarix, and Pentacel); 44,061 (95%) of the reports involved children aged <6 years. DTaP vaccine was administered concurrently with one or more other vaccines in 40,868 (88%) case reports (CDC, unpublished data, 2016). The median time from vaccination to onset of an adverse event was 1 day. The most frequently reported adverse events were injection-site erythema (11,879 [26%]), pyrexia (9,225 [20%]), injection-site swelling (6,964 [15%]), erythema site other than injection site or site not specified (5,339 [12%]), and injection-site warmth (4,468 [10%]). When VAERS DTaP reports for each vaccine brand were compared individually with those for all other inactivated vaccines in the VAERS database, no concerning patterns of adverse events were observed.

Among all DTaP vaccine-related reports, 5,205 (11%) were coded as serious (i.e., one of the following outcomes was reported: death, life-threatening illness, hospitalization, prolongation of hospitalization, or permanent disability). Among those reports coded as serious, the most frequent adverse events were pyrexia (1,795 [35%]), vomiting (1,420 [27%]), irritability (1,101 [21%]), seizure (938 [18%]), and intussusception (746 [14%]). In 97% of the 728 intussusception reports, rotavirus vaccine was administered concomitantly. Intussusception has been associated with administration of both U.S.-licensed rotavirus vaccine products (*126*,*127*).

A total of 793 deaths following receipt of DTaP vaccines were reported in VAERS during the study period (CDC, unpublished data, 2016). An autopsy report or other type of medical record was available for 682 (86%) reports and reviewed for cause of death. The most frequent reported cause of death was sudden infant death syndrome (SIDS) in 338 (49.6%) reports. Other categories of death included asphyxiation (47 [6.8%]); diseases of the respiratory system (44 [6.5%]); diseases of the circulatory system (27 [3.9%]); certain infections or parasitic diseases (27 [3.9%]); diseases of the nervous system (24 [3.5%]); and congenital malformations, deformations and chromosomal abnormalities (23 [3.4%]). In 90 (13.2%) death reports, the cause was undetermined and in 62 (9.1%) death reports various other causes were reported (e.g., blunt force trauma). These reported frequencies are similar to those observed with overall U.S. infant mortality data and among recipients of other recommended childhood vaccines (*128*). Two recent VSD studies do not suggest a causal relation or increased risk for death following vaccination of any type (*129*,*130*).

Adverse Events Associated with Vaccines with Pertussis Components or Tetanus Toxoid–Containing Components

Vaccines with Pertussis Components

Because of concerns about the possible role of vaccines with acellular pertussis components in causing neurologic reactions or exacerbating underlying neurologic conditions, ACIP recommendations to defer pertussis vaccines in infants with suspected or evolving neurologic disease, including seizures, have been based primarily on concerns that neurologic events after vaccination (with whole-cell preparations in particular) might interfere with the subsequent evaluation of the infant's neurologic status (*3*,*12*,*131*).

During the whole-cell pertussis vaccine era, the Institute of Medicine (IOM) concluded that evidence favored acceptance of a causal relation between pediatric DTP use and acute encephalopathy (*132*). After the change to DTaP vaccines, IOM reviewed the evidence for a causal association between acellular pertussis–containing vaccines and several neurologic outcomes (*133*). The evidence was inadequate to accept or reject a causal relation between receipt of acellular pertussis-containing vaccine and encephalitis, encephalopathy, infantile spasms, seizures, ataxia, autism, acute disseminated encephalomyelitis, transverse myelitis, optic neuritis, onset of multiple sclerosis in adults, relapse of multiple sclerosis in adults, relapse of multiple sclerosis in children, Guillain-Barré syndrome, chronic inflammatory disseminated polyneuropathy, opsoclonus myoclonus syndrome, or Bell's palsy (*133*).

Pediatric DTaP is contraindicated in children with a history of encephalopathy not attributable to another identifiable cause occurring within 7 days after pediatric DTP/DTaP vaccination (Table 2). Although active surveillance in Canada among a population of children administered 6.5 million doses of pertussis vaccines during 1993–2002 failed to ascertain any acute encephalopathy cases causally related to whole-cell or

acellular pertussis vaccines, postlicensure surveillance in Japan during a 23 year period demonstrated rates of encephalopathy/encephalitis (death) of 7.6 cases within 7 days of vaccination per 10 million doses during 1970–1974 when DTP was administered, and 0.5 cases per 10 million doses during 1989–2000 when DTaP replaced DTP (*113*,*134*).

ACIP recommends that infants with evolving neurologic conditions not be vaccinated with pediatric DTaP until a treatment regimen has been established and the condition has stabilized (Table 2) (*3*). A history of seizures (febrile or afebrile) <3 days after a previous dose of DTP/DTaP, a history of well-controlled seizures in the vaccinee or a family history of seizures or other neurologic disorder is not a contraindication or precaution to vaccination with pertussis components (Table 3) (*3*).

Hypotonic-hyporesponsive episodes (HHE) and prolonged crying are adverse events that are less commonly reported with DTaP than were historically reported with DTP (*111*,*135*,*136*). Neither HHE nor prolonged crying after receipt of DTP/DTaP are known to be associated with serious sequelae, and both adverse events have been reported after receipt of vaccines other than DTP/DTaP (*135*,*136*). Among children who received subsequent DTP/DTaP doses, recurrent HHE occurrences are very rarely reported (*135*,*136*). A single, uncomplicated occurrence of either HHE or prolonged crying does not preclude vaccination, and the benefits of vaccination outweigh the risks for additional episodes.

ACIP recommends that vaccine providers and parents evaluate the risks for and benefits of administering subsequent doses of vaccines with pertussis components to young children who after receiving pediatric DTP/DTaP experienced any of the events listed in the table for contraindications and precautions for DTaP, DT, Td, or Tdap vaccines (Table 2). All of these events were documented more frequently following whole-cell pertussis vaccines than following acellular vaccines (*3*,*110*,*111*,*136*,*137*).

Tetanus Toxoid–Containing Vaccines

As with the recent conclusions regarding acellular pertussis–containing vaccines, IOM also concluded that the evidence was inadequate to accept or reject a causal relation between receipt of diphtheria toxoid and tetanus toxoid–containing vaccine and encephalitis, encephalopathy, infantile spasms, seizures, ataxia, autism, acute disseminated encephalomyelitis, transverse myelitis, optic neuritis, onset of multiple sclerosis in adults, relapse of multiple sclerosis in adults, relapse of multiple sclerosis in children, Guillain-Barré syndrome, chronic inflammatory disseminated polyneuropathy, opsoclonus myoclonus syndrome, or Bell's palsy (*133*). ACIP recommends that Guillain-Barré syndrome occurring <6 weeks after receipt of a tetanus toxoid–containing vaccine is a precaution for subsequent administration of tetanus toxoid–containing vaccines (*52*).

IOM has concluded that evidence from case reports and uncontrolled studies involving tetanus toxoid–containing vaccines favored a causal relation between tetanus toxoid–containing vaccines and brachial neuritis (*133*). Although brachial neuritis is considered to be a compensable event through the Vaccine Injury Compensation Program (VICP), ACIP considers that occurrence of brachial neuritis following vaccination with a tetanus toxoid–containing vaccine does not preclude their future use in the same person; brachial neuritis is usually self-limited (*52*,*132*,*138*).

Milk Allergy

DTaP and Tdap vaccines might include residual milk allergens from ingredients used during manufacturing (*139*). Because of reports of children and adolescents with a documented history of severe milk allergy having an anaphylactic reaction to booster doses of DTaP or Tdap within one hour of administration (*139*,*140*), a prospective review of VAERS data was conducted. No safety signal in VAERS for anaphylaxis in patients with milk protein allergy was identified, leading to the conclusion that these vaccines are tolerated by those with a milk allergy, and that milk allergy is not a contraindication or precaution to receipt of DTaP or Tdap (*140*); vaccine providers should continue to vaccinate persons with milk allergy as recommended and strongly consider monitoring the patient for anaphylaxis.

Simultaneous Administration of DTaP with Other Vaccines

Simultaneous administration of vaccines is defined as administering more than one vaccine on the same clinic day, at different anatomical sites, and not combined in the same syringe (*52*). Before the availability of DTaP-containing combination vaccines, administration of DTaP vaccine was recommended with other vaccines on the same clinic day. Limited historic data regarding simultaneous administration of the first 3 doses of DTaP with other childhood vaccines indicate no interference with response to any of these antigens (*3*).

A recent safety study on simultaneous administration of DTaP with other vaccines indicated a small increased risk for febrile seizures during the 24 hours after a child receives the inactivated influenza vaccine (IIV) at the same time as the pneumococcal 13-valent conjugate (PCV13) vaccine or DTaP (*123*). Other studies have not shown an increased risk for febrile seizures after DTaP, except when simultaneously administered with IIV (*114*,*115*,*121*,*122*). The risk for febrile seizure with any combination of these vaccines is small; ACIP recommends simultaneous administration of these vaccines.

Tdap Vaccines

Two Tdap products are licensed for use in adolescents and adults as a single-dose booster vaccination against tetanus, diphtheria, and pertussis: Boostrix (GlaxoSmithKline, Rixensart, Belgium), and Adacel (Sanofi Pasteur, Swiftwater, Pennsylvania). The age indication for approved use differs depending upon the specific Tdap product and licensure (Table 5). Both Tdap products consist of pertussis antigen and diphtheria and tetanus toxoids (Table 5). The pertussis antigen composition and amount differ, as does the amount of diphtheria toxoids between the two Tdap products. Summaries of the data on the immunogenicity and safety of each of these vaccines have been published (*4*,*5*).

Adacel (Sanofi Pasteur) is licensed by FDA as a single dose in persons aged 10–64 years (*141*). Adacel contains the same tetanus toxoid, diphtheria toxoid, and five pertussis antigens (PT, PRN, FHA, and FIM) as those in Daptacel (pediatric DTaP), but is formulated with reduced quantities of the toxoids and antigens (Table 5). Adacel contains no thimerosal or other preservative. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142764.pdf).

Boostrix (GSK) is licensed by FDA as a single dose in persons aged ≥10 years (*142*). Boostrix contains the same tetanus toxoid, diphtheria toxoid, and three pertussis antigens (PT, PRN, and FHA) as those in Infanrix (pediatric DTaP), but is formulated with reduced quantities of the toxoids and antigens (Table 5). Boostrix contains no thimerosal or other preservative. Additional information is available in the package insert (https://www.fda.gov/downloads/BiologicsBloodVaccines/UCM152842.pdf).

Immunogenicity and Efficacy

Both Tdap products were licensed on the basis of clinical trials demonstrating immunogenicity not inferior to U.S.-licensed Td or pediatric DTaP products and an overall safety profile clinically comparable to U.S.-licensed Td products (*143*,*144*). Determining the efficacy of the tetanus and diphtheria toxoid components for each Tdap product was based on the comparison of the rates of protective immune response to these antigens as compared to U.S.-licensed Td and using established serologic correlates of protection (*45*,*72*). The percentage of persons achieving protective antitetanus and antidiphtheria antibody concentrations (>0.1 IU/mL) and the booster response to each of these antigens 1 month postvaccination were evaluated.

Because no well-accepted serologic or laboratory correlate of protection against pertussis has been established, clinical endpoint efficacy studies of acellular pertussis vaccines among adolescents or adults were not required for Tdap licensure. Instead, the efficacy of the pertussis components of Tdap vaccines was inferred using a serologic bridge to infants vaccinated with DTaP in efficacy trials with clinical endpoints (*145*). The immune response of adolescents and adults to each pertussis vaccine antigen after a single dose of Tdap was compared with the immune responses of infants who received 3 doses of pediatric DTaP that included the same pertussis components as the Tdap being assessed (*141*,*142*). The percentage of persons with an acceptable booster response to pertussis vaccine antigens according to predefined criteria also was evaluated. The predefined lower limit was defined as the lower limit of 95% CI for the GMC ratio of the Tdap/pediatric DTaP. Prelicensure Tdap vaccine efficacy was inferred using a serologic bridge to infants vaccinated with 3 doses of DTaP and ranged from 79% to 89% (*105*,*106*).

Postlicensure Tdap Effectiveness

Following the 2005 Tdap recommendation for adolescents and adults, postlicensure pertussis vaccine effectiveness estimates for Tdap in settings with similar vaccines and recommendation schedules have ranged from 66% to 78% among adolescents who received both DTP and DTaP as children (*146*–*148*). Among adolescents who received only DTaP as children, in a matched case-control study, the overall estimated vaccine effectiveness of Tdap against pertussis was 63.9% (95% CI = 50%–74%) (*29*). Initial vaccine effectiveness against pertussis within one year of Tdap vaccination was 73% (95% CI = 60%–82%), but after 2–4 years, postvaccination vaccine effectiveness decreased to 34% (95% CI = -0.03%–58%) (*29*). Another study that calculated Tdap vaccine effectiveness among adolescents found that, within the first year after vaccination, effectiveness was 68.8% (95% CI = 59.7%–75.9%); by ≥4 years after vaccination, vaccine effectiveness was 8.9% (95% CI = -30.6%–36.4%) (*149*). As observed with DTaP, Tdap vaccine effectiveness declines substantially with increasing time since vaccination (*29*,*149*,*150*). Although there are no studies estimating Tdap vaccine effectiveness in persons who received only DTP as infants, reported rates of pertussis have been observed to be significantly lower among children who had started their vaccination series with DTP than among those who had started with DTaP (*151*,*152*).

Prevention of Transmission: Indirect Protection ("Cocooning")

At the time Tdap was first recommended, it was anticipated that this vaccine would prevent pertussis in adolescents and adults and thereby result in preventing transmission

of *B. pertussis* to contacts (e.g., infants). Providing indirect protection through Tdap vaccination to adults was the premise for the "cocooning" strategy to prevent pertussis in young infants at highest risk for severe pertussis morbidity and mortality. A limited number of studies have evaluated the effectiveness of Tdap vaccination in preventing transmission of pertussis in young infants, but the evidence was inconclusive. Although one study found a modest decrease in the risk for pertussis in infants whose mothers received postpartum Tdap, another study found that mother's postpartum vaccination and cocooning did not reduce pertussis in infants (*153*,*154*).

Studies in animal models have shown that acellular pertussis vaccines protect against disease but not against infection or transmission of *B. pertussis* or the closely related species, *B. bronchiseptica* (*155*–*157*). Although it is unclear if these animal models fully represent human disease, expert opinion is that persons vaccinated with acellular pertussis vaccines can become infected with and transmit *B. pertussis* (*158*,*159*). Persons up to date with pertussis vaccines are less likely to have severe disease compared with those not up to date (*160*). Although it is presumed that vaccinated persons with less severe disease would be less likely to transmit *B. pertussis* because of less frequent or severe coughing, more recent evidence suggests that vaccination with acellular pertussis vaccines does not prevent transmission and therefore does not afford indirect protection against pertussis (*155*–*157*).

Postlicensure Safety of Tdap

Since 2005, when both Tdap products were first licensed and recommended, both vaccine product label indications have expanded and ACIP Tdap recommendations have been updated (*6*,*8*–*10*,*161*–*163*). A summary of these recommendations is available at https://stacks.cdc.gov/view/cdc/52821. Routine VAERS surveillance for and VSD studies on adverse events following receipt of Tdap vaccines in persons aged 10–64 years have provided reassuring data that support the prelicensure clinical trial safety data and have not demonstrated any associations between Tdap and the following rare adverse events: encephalopathy-encephalitis-meningitis; paralytic syndromes; seizures; cranial nerve disorders; and Guillain-Barré syndrome (*164*–*166*). Medically attended local reactions were uncommon and did not differ with concomitant or sequential administration of diphtheria toxoid–containing vaccines (Td/Tdap and MenACWY-D [meningococcal serogroups A, C, W, and Y] Menactra, Sanofi Pasteur) (*167*). No increased risk for medically attended neurologic or allergic reactions was observed following Tdap vaccination and, when compared with matched historical Td recipients, no increase in the onset of new chronic illnesses was seen after Tdap (*168*). Although a 2016 study found an increased risk for acute disseminated encephalomyelitis following Tdap vaccination, this finding was based on cases in two Tdap-vaccinated persons and might have been unrelated to vaccination (*169*). Safety data from VAERS, VSD, and other studies in populations not originally routinely recommended to receive Tdap (e.g., adults aged ≥65 years and pregnant women) have become available since 2009 and were reviewed by ACIP (*6*,*8*–*10*).

Persons Aged ≥65 Years

For adults aged ≥65 years, Tdap vaccine safety was comparable to that of Td vaccine (*170*,*171*). The most frequent adverse events following receipt of Tdap in persons aged ≥65 years were local injection-site reactions, and no unusual or unexpected clusters of adverse events after Tdap were identified (*170*). In addition, the risks for the following prespecified events were comparable following receipt of Tdap and Td in older persons: meningitis, encephalitis and encephalopathy; cranial nerve disorders, including Bell's palsy; Guillain-Barré syndrome; brachial neuritis; paralytic syndromes; medically attended inflammatory or allergic events; and anaphylaxis and generalized reactions (*171*).

Interval of Tdap After Td

When Tdap was licensed in 2005, the safety of administering a dose of Tdap at intervals <5 years after Td or pediatric DTP/DTaP had not been studied. Evaluations of the safety of administering Tdap at intervals <5 years after Td, including as short as 18 months, suggest that the safety of much shorter intervals is acceptable (*172*–*174*). Two studies were conducted in adults who received a Tdap or combined Tdap-inactivated polio (Tdap-IPV) vaccine <2 years following a previous Td-containing vaccine (*173*,*174*). Observed adverse events were limited to local reactions, including pain (68%–83%), erythema (20%–25%), and swelling (19%–38%) (*173*,*174*). Although serious adverse events did not occur, the numbers of subjects in these studies were small and the potential for rare, but serious, adverse events cannot be excluded. ACIP concluded that although longer intervals between Td and Tdap vaccination could decrease the occurrence of local reactions, the benefits of protection against pertussis outweigh the potential risk for adverse events (*8*).

Persons Aged 7–10 Years

ACIP concluded that the overall safety of Tdap and the frequency of local reactions in persons aged 7–10 years who have not completed the childhood DTaP series likely would be similar to those observed in children who received 4 doses of DTaP (*8*). Although both Tdap products are approved for use in persons as young as age 10 years, no data have been published regarding the safety of Tdap in children aged 7–9 years who

have never received pertussis-containing vaccines. Several studies assessing the safety and immunogenicity of Tdap or Tdap-IPV as the fifth dose of acellular pertussis vaccine in children aged 4–8 years were reviewed (*175–179*). No increase in the risk for severe local reactions or systemic adverse events was observed (*175–179*). The most commonly reported adverse events that occurred within 15 days after receipt of Tdap were pain (40%–56%), erythema (34%–53%), and swelling (24%–45%). Fewer local reactions were observed or reported among Tdap or Tdap-IPV recipients compared with those who received DTaP or DTaP-IPV, but the differences were not statistically significant. No differences were noted when children aged 4–6 and 7–8 years were compared with respect to the frequency of solicited or unsolicited adverse reactions following vaccination with Tdap-IPV (*179*).

Pregnant Women

In 2011, when ACIP first considered administration of Tdap during pregnancy, safety data on women and their infants were limited (*9*); prelicensure evaluations did not study the safety of administering a booster dose of Tdap to pregnant women. ACIP reviewed available data from VAERS, pregnancy registries established by both Sanofi Pasteur (Adacel) and GSK (Boostrix), and small studies (*174,180–183*). ACIP concluded that these studies did not suggest any elevated risk for or unusual patterns of adverse events in pregnant women who received Tdap or in their newborn infants, and the few serious adverse events reported were judged unlikely to have been caused by the vaccine (*9*). A summary of these studies is available at https://stacks.cdc.gov/view/cdc/52820.

When ACIP considered recommending Tdap vaccination during each pregnancy, the safety information concerning booster doses of Tdap in pregnant women previously vaccinated with Tdap was not available (*6*). Data on the safety of two closely spaced doses of tetanus toxoid–containing vaccines were limited to receipt of Td and Tdap or Tdap-IPV vaccine within 21 days or ≤2 years and receipt of 2 doses of Tdap at a five-year interval in nonpregnant persons; of the few serious adverse events reported, none were attributed to the vaccine (*172–174,184,185*). Receipt of a second dose of Tdap in nonpregnant persons was well tolerated; injection-site pain was the most commonly reported adverse event (*184–188*). The frequency of reported adverse events following the second dose of Tdap was similar to that after the first dose in the same subjects and in controls receiving Tdap for the first time.

A theoretical risk for severe local reactions exists among pregnant women who are vaccinated during multiple closely spaced pregnancies. These severe local reactions are hypersensitivity reactions that have been associated with vaccines containing tetanus toxoid, tetanus, and diphtheria toxoids and/or pertussis antigens in persons who have received multiple doses of vaccine. Most of the data on multiple doses of tetanus toxoid–containing vaccines and hypersensitivity reactions are historical, and the risk for severe adverse events likely has been reduced with current formulations that contain lower concentrations of tetanus toxoid (*45,189,190*). Recent studies were small and did not include pregnant subjects; therefore, the findings do not exclude the possibility of rare but serious adverse events in pregnant women after receipt of Tdap (*6*).

ACIP recognized the need for safety studies of severe adverse events when Tdap is administered during subsequent pregnancies but concluded that the potential benefit of preventing pertussis morbidity and mortality in infants too young to be fully vaccinated outweighs the theoretical concern of possible localized severe adverse events in pregnant women receiving Tdap. ACIP also concluded that experience with tetanus toxoid–containing vaccines suggests no excess risk for severe adverse events among women receiving Tdap with each pregnancy (*6*).

Additional data from the United States and elsewhere on the safety of Tdap vaccination during pregnancy for both pregnant women and their infants continue to be reassuring, with no reported increase in adverse events, including adverse birth outcomes, and no observation of new or unexpected vaccine safety concerns (*191–209*); a summary of these studies is available at https://stacks.cdc.gov/view/cdc/52820. Receipt of Tdap during pregnancy has not been found to be associated with an increased risk for frequency of major malformations, stillbirth, preterm birth, small for gestational age, or hypertensive disorders (*193–195,197,208*). One study observed a slight increase in the risk for chorioamnionitis and, although chorioamnionitis is a risk factor for preterm birth, there were no associated increases in preterm or small for gestational age births in this cohort (*193*). The authors concluded that the small increase in the risk for chorioamnionitis was likely due to residual confounding or heterogeneity in outcome ascertainment (*193*). A review of the VAERS database from 1990 through 2014 found 31 reports of chorioamnionitis following receipt of any vaccine out of 3,389 pregnancy reports (*198*).

An evaluation of the safety of Tdap and influenza vaccines administered concomitantly and sequentially to pregnant women aged 14–49 years found no statistically significant increase in risk for fever or any medically attended acute adverse event in pregnant women vaccinated concomitantly compared with sequentially. No differences in preterm delivery, low birth weight, or small for gestational age neonates were observed between the two groups (*196*).

Data on the safety of receipt of Tdap during pregnancy in close intervals from prior tetanus toxoid–containing

vaccinations are limited. One study found no increased risk for acute adverse events (i.e., fever, allergy, and local reactions) or adverse birth outcomes (i.e., small for gestational age, preterm delivery, and low birth weight) for those women who had a previous vaccination ≤5 years before compared with those vaccinated >5 years before receipt of Tdap during pregnancy, suggesting that recent receipt of a prior tetanus toxoid–containing vaccination does not increase risk for adverse events after Tdap vaccination in pregnancy (*195*).

Additional Safety Data

Neurologic and Systemic Events Associated with Vaccines with Pertussis Components

Concerns about the possible role of vaccines with pertussis components in causing neurologic reactions or exacerbating underlying neurologic conditions are long-standing (*12*,*131*). Although the occurrence of neurologic sequelae after receipt of vaccines with pertussis components is rare, the evidence for a causal association between acellular pertussis–containing vaccines and neurologic outcomes is inconclusive (*133*). Concerns about vaccinating adolescents with progressive or uncontrolled underlying neurologic disease must be weighed against the potential morbidity of pertussis; adolescents with severe neurologic conditions might be at risk for severe pertussis (CDC, unpublished data, 2005) (*39*). ACIP does not consider a history of well-controlled seizures in the vaccinee or a family history of seizures (febrile or afebrile) or other neurologic disorder to be a contraindication or precaution to vaccination with pertussis components (Table 3) (*3*).

ACIP recommends that the risks for and benefits of administering subsequent doses of vaccines with pertussis components be evaluated for young children who, after receiving pediatric DTP/DTaP, experienced any of the events listed in the table as contraindications and precautions for DTaP, DT, Td, and Tdap vaccines (Table 2); all of these events were documented more frequently following whole-cell pertussis vaccines than following acellular vaccines (*3*,*110*,*111*,*136*,*137*). For adolescents and adults, these events (e.g., febrile seizures and HHE) either do not occur or are of less clinical concern than such events in infants and children. Taken together, this information supports administering Tdap to adolescents with a history of the events listed under pediatric DTaP/DTP (Table 2).

ACIP recommends that adolescents with unstabilized progressive neurologic conditions not be vaccinated with Tdap until the condition stabilizes. However, progressive neurologic disorders that are chronic and stable (e.g., dementia) are more common among adults, and the possibility that Tdap would complicate subsequent neurologic evaluation is of less clinical concern. As a result, chronic progressive neurologic conditions that are stable in adults do not constitute a reason to delay Tdap; this is in contrast to unstable or evolving neurologic conditions (e.g., cerebrovascular events and acute encephalopathic conditions) (*5*).

Arthus Reactions

Arthus reactions (type III hypersensitivity reactions) are rarely reported after vaccination, but can occur after tetanus toxoid- or diphtheria toxoid–containing vaccines (CDC, unpublished data, 2005) (*54*,*132*,*210*–*214*). An Arthus reaction is a local vasculitis associated with deposition of immune complexes and activation of complement. Immune complexes form in the setting of a high local concentration of vaccine antigens and high concentration of circulating antibody (*210*,*211*,*213*,*215*). Arthus reactions are characterized by severe pain, swelling, induration, edema, hemorrhage, and occasionally necrosis. These symptoms and signs usually occur 4–12 hours after vaccination; by contrast, anaphylaxis (an immediate type I hypersensitivity reaction) usually occurs within minutes of vaccination. As with extensive limb swelling, Arthus reactions usually resolve without sequelae. ACIP recommends that persons who have experienced an Arthus reaction following a dose of tetanus toxoid or diphtheria toxoid–containing vaccine should not receive a tetanus toxoid–containing vaccine more frequently than every 10 years, even for tetanus prophylaxis as part of wound management (*54*).

Tetanus Toxoid Safety

Tetanus toxoid is one of the most extensively used vaccines globally, either as a monocomponent vaccine (TT) or combined with diphtheria toxoid (DT and Td) and pertussis antigens (DTP, DTaP, and Tdap). Historically, mild local reactions (i.e., redness, pain and tenderness, and mild swelling) after receipt of TT vaccine are common (0–95%). Systemic reactions (i.e., fever, malaise, headache, and lymphadenopathy) are less common but might occur, particularly after receipt of a booster dose of vaccine. Severe reactions, including neurologic (e.g., peripheral neuropathy, particularly brachial plexus neuropathy, Guillain-Barré syndrome, seizures, and acute encephalopathy) and hypersensitivity reactions (anaphylaxis) are exceedingly rare (*45*,*216*).

An evaluation by IOM concluded that evidence from case reports and uncontrolled studies involving tetanus toxoid–containing vaccines favored a causal relation between tetanus toxoid–containing vaccines and brachial neuritis (*133*). Although brachial neuritis is considered to be a compensable event through the National Vaccine Injury Compensation Program (VICP), ACIP considers that occurrence of brachial neuritis following vaccination with a tetanus toxoid–containing

vaccine does not preclude their future use in the same person; brachial neuritis is usually self-limited (*52*,*132*,*138*).

As with the recent conclusions regarding acellular pertussis–containing vaccines, IOM also concluded that the evidence was inadequate to accept or reject a causal relation between receipt of diphtheria toxoid- and tetanus toxoid–containing vaccine and encephalitis, encephalopathy, infantile spasms, seizures, ataxia, autism, acute disseminated encephalomyelitis, transverse myelitis, optic neuritis, onset of multiple sclerosis in adults, relapse of multiple sclerosis in adults, relapse of multiple sclerosis in children, Guillain-Barré syndrome, chronic inflammatory disseminated polyneuropathy, opsoclonus myoclonus syndrome, or Bell's palsy (*133*). ACIP considers Guillain-Barré syndrome occurring <6 weeks after receipt of a tetanus toxoid–containing vaccine a precaution for subsequent administration of tetanus toxoid–containing vaccines (*52*). Active surveillance data covering two million doses of Tdap administered to both adolescent and adult populations failed to demonstrate an association between receipt of a tetanus toxoid–containing vaccine and onset of Guillain-Barré syndrome within six weeks following vaccination (*164*,*165*,*217*).

Pregnant Women

Tetanus toxoid–containing vaccines are safe in pregnant women. No evidence exists to indicate that tetanus and diphtheria toxoids administered during pregnancy are teratogenic (*54*). Field trials of tetanus toxoid in pregnant women have shown high efficacy (80%–100%) in preventing maternal and neonatal tetanus (*50*,*218*–*222*).

Arthritis

Although the causal relation between vaccination with tetanus toxoid and arthritis is biologically plausible, the evidence of a possible association between receipt of tetanus vaccine and arthritis is limited (*132*). In 1994, on the basis of case reports, case series and uncontrolled observational studies, IOM concluded that the evidence was insufficient to demonstrate a causal link between receipt of tetanus toxoid and arthritis (*132*). In a second review of the evidence, IOM reached a similar conclusion on the basis of several case reports and two case-control studies (*133*). The first case-control study found an increased risk for psoriatic arthritis after tetanus toxoid vaccination (odds ratio [OR]: 1.91; 95% CI = 1.0%–3.7%) (*223*). In the second study, the investigators concluded that tetanus toxoid or diphtheria vaccination did not increase the risk for rheumatoid arthritis (*224*). Both studies had serious limitations and low precision (*133*).

A more recent study in a large health maintenance organization assessed the risk for rheumatoid arthritis after tetanus, influenza, and hepatitis B vaccination, using a cohort and case-control design to determine risk at different intervals postvaccination (*225*). This study did not identify a significantly increased risk for rheumatoid arthritis associated with tetanus vaccine for any interval assessed (*225*).

Diphtheria Toxoid Safety

Reactogenicity with vaccines containing diphtheria toxoid is common. All available pertussis-containing vaccines include diphtheria toxoid, and different forms of diphtheria toxoid are used as carrier proteins in certain conjugate vaccines (MenACWY-D [Menactra, Sanofi Pasteur], MenACWY-CRM [Menveo, GlaxoSmithKline, Rixensart, Belgium], 13-valent pneumococcal polysaccharide-protein conjugate vaccine [PCV13, Prevnar13, Wyeth Pharmaceuticals Inc., Collegeville, Pennsylvania, a subsidiary of Pfizer Inc., New York, New York]). The frequency of reported adverse events from diphtheria toxoid–containing vaccines varies by vaccine formulation, dose of diphtheria toxoid, prior vaccination history, and prevaccination antidiphtheria toxoid antibody levels. Although local injection-site reactions are common, only a small proportion of these are clinically significant (*226*). Administration of diphtheria toxoid has not been associated with anaphylaxis.

Because diphtheria toxoid is not administered as a monovalent diphtheria toxoid vaccine, it is difficult to characterize reactogenicity to diphtheria toxoid alone. However, in a study of 180 persons comparing the reactogenicity of DTaP (diphtheria toxoid ≥10 IU) with that of Td (diphtheria toxoid ≥2 IU) and of monovalent diphtheria toxoid (diphtheria toxoid ≥2 IU), the proportion of vaccinees with local reactions (e.g., erythema, induration, warmth, and tenderness) was generally lower among recipients of the monovalent diphtheria toxoid than was observed in the other two groups (*227*). There was no consistent pattern of increased reactogenicity among recipients of DTaP compared with Td (*227*). In addition, data from several controlled studies suggest that fever and local reactions are more common after administration of Td than after TT vaccine (*190*,*228*,*229*). In general, the frequencies of reported common systemic signs and symptoms in infants (i.e., temperature of ≥38° C [≥100.4° F], crying for ≥1 hour, irritability, drowsiness, loss of appetite, and vomiting) and local reactions (i.e., redness, swelling, and tenderness) after vaccination with DT or DTaP were comparable (*230*).

Pregnant Women

Diphtheria toxoid–containing vaccines are safe in pregnant women. No evidence exists to indicate that tetanus and diphtheria toxoids administered during pregnancy are teratogenic (*54*). Randomized trials of diphtheria toxoid conducted among pregnant women in the 1940s demonstrated efficient

transplacental transfer of maternal antidiphtheria antibodies and protection of infants against diphtheria (*231–234*).

Simultaneous Administration of Tdap with Other Vaccines

Pre- and postlicensure studies in adolescents and adults have evaluated and support the safety and immunogenicity of Tdap when administered simultaneously or sequentially with one or two other vaccines (e.g., MenACWY, HepB, and human papillomavirus [HPV] and trivalent inactivated influenza vaccines) (*141*,*167*,*235–242*). In most of these studies, no differences were observed in the safety profiles when Tdap was administered simultaneously or sequentially with another vaccine. However, the rates of erythema and swelling at the Tdap injection site were higher when it was co-administered with HepB vaccine (*141*). Swollen or sore joints were reported in both the simultaneous (22.5%) and sequential (17.9%) vaccination groups, with most joint complaints being mild in intensity and lasting a mean duration of 1.8 days (*141*).

Tdap was immunogenic when administered simultaneously with other vaccines. The proportions of subjects achieving protective levels of antibodies against diphtheria and tetanus were similar in the simultaneously vaccinated group compared with those vaccinated sequentially (*235–242*). Immune responses to pertussis antigens were similar when Tdap was administered simultaneously or sequentially with MenACWY-D, HPV (bivalent or quadrivalent) or HepB vaccines, although the immune responses to pertussis antigens with MenACWY-CRM (Menveo, Novartis) and trivalent inactivated influenza vaccines were lower after simultaneous administration (*141*,*235–241*). When Tdap was administered simultaneously with MenACWY-CRM (Menveo, Novartis), the immune responses to two of the three pertussis antigens were lower, but the clinical relevance of this finding, if any, is not clear (*237*). When Tdap and trivalent inactivated influenza vaccines were administered to adults aged 19–64 years, the immune responses to the pertussis antigens were lower but noninferior in the simultaneously vaccinated group compared with the immue responses to the pertussis antigens in those vaccinated sequentially, with the exception of Adacel's PRN and Boostrix's FHA and PRN (*235*,*236*). The clinical significance, if any, of not meeting noninferiority criteria for these antigens is unclear (*235*). For adults aged ≥65 years, compared with separate administration of Boostrix and a trivalent inactivated influenza vaccine, simultaneous administration of these two vaccines also was safe and immunogenic (*242*).

Cost-Effectiveness Analyses

As part of the consideration of recommendations for use of Tdap in specific populations, cost-effectiveness analyses were conducted for specific vaccination strategies and target populations. These were considered for adults aged ≥65 years and women during pregnancy.

Vaccinating Adults Aged ≥65 Years

Two cost-effectiveness analyses of the epidemiologic and economic impact of substituting a single dose of Tdap for one decennial Td booster in healthy persons aged ≥65 years were reviewed by ACIP (CDC, unpublished data, 2012) (*243*). Both models were developed to assess the epidemiologic and economic impact of Tdap vaccination in adults aged ≥65 years, and both demonstrated that a dose of Tdap administered to older adults resulted in a modest decrease in the number of cases of pertussis and other outcomes (e.g., outpatient visits, hospitalizations, and deaths) (CDC, unpublished data, 2012) (*243*). From the two models with similar incidence (100–104 cases per 100,000 population), the cost per quality adjusted life-year saved ranged from $30,946 to $62,716 and the cost per case averted ranged from $1,966 to $3,263 (CDC, unpublished data, 2012) (*243*). Model results were most sensitive to the incidence of pertussis; however, sensitivity analyses showed that, even assuming a range of estimates of pertussis underreporting, Tdap vaccination compared with no Tdap vaccination might be cost-effective in this population. Reassured by the concordance between the two cost-effectiveness models, ACIP's conclusion was that the cost per case averted and the cost per quality-adjusted life-year saved were modest (*10*).

Maternal Tdap Vaccination and Cocooning

A decision and cost-effectiveness model was developed to assess the likely impact and cost-effectiveness of Tdap vaccination administered during pregnancy versus postpartum with or without cocooning. The model showed that Tdap vaccination during pregnancy could reduce annual infant pertussis incidence more than postpartum vaccination, reducing cases by 33% versus 20%, hospitalizations by 38% versus 19%, and deaths by 49% versus 16%. The cost per quality adjusted life-year saved for pregnancy vaccination was $414,523 compared with postpartum vaccination, which was $1,172,825. The two primary drivers of the reduction in infant pertussis were earlier indirect protection from the mother by vaccinating before the infant's birth and the provision of passive immunity to the infant through transplacental transfer of maternal antibodies. Sensitivity analyses under robust conditions, including reduced Tdap vaccine effectiveness, did not alter the relative benefits of vaccination during pregnancy (*244*).

Strategy for Pertussis, Tetanus, and Diphtheria Control

Routine DTaP, Tdap, and Td Vaccination

In the United States, reported tetanus and diphtheria cases are rare. Although vaccine coverage is high among infants, children, and adolescents, serologic and survey data indicate that adults are undervaccinated against tetanus and diphtheria and that coverage declines with increasing age (*36*,*51*). Maintaining seroprotection against tetanus and diphtheria through adherence to the ACIP-recommended schedule of booster doses of vaccine is important for adults of all ages.

In contrast to tetanus and diphtheria, the incidence of reported pertussis in the United States has been increasing despite high infant and childhood coverage with DTaP vaccines and increasing Tdap coverage among adolescents (*245*). Although vaccine-induced protection provided by acellular pertussis vaccines wanes over time, vaccination remains the best protection available against pertussis. ACIP recognizes that not all cases of pertussis can be prevented. However, sustaining vaccine coverage in young children (DTaP) and adolescents (Tdap) with the available licensed vaccines and achieving high Tdap coverage among adults, especially pregnant women, presents the best available means of preventing pertussis.

Preventing Pertussis in Young Infants Through Maternal Tdap Vaccination

Because young infants continue to be at greatest risk for hospitalization and death due to pertussis, ACIP has made efforts to optimize the vaccination program strategies for preventing pertussis in those too young to be vaccinated. Very young infants are dependent in part on passively acquired maternal antibodies, which are thought to protect infants from infection and to modify the severity of diverse infectious diseases in infants for varying periods of time (*246*,*247*). Before the ACIP recommendation to vaccinate pregnant women, several studies provided evidence supporting the existence of efficient transplacental transfer of pertussis antibodies (*181*,*248*,*249*). These studies indicated that newborn infants whose mothers received Tdap before or during pregnancy had higher concentrations of pertussis antibodies at birth compared with those of unvaccinated mothers (*181*,*248*,*249*).

The strategy of preventing pertussis in newborns through the vaccination of women with Tdap during pregnancy from 27 through 36 weeks' gestation is 80%–91% effective (CDC, unpublished data, 2016) (*250–253*). One study found that, among infants infected with pertussis, those born to mothers vaccinated with Tdap during pregnancy had less severe pertussis than those born to unvaccinated mothers; maternal vaccination was 58% effective in preventing hospitalization among infants infected with pertussis (*254*).

Vaccinating From 27 Through 36 Weeks' Gestation

Tdap may be administered any time during pregnancy, but vaccination during the third trimester likely provides the highest concentration of maternal antibodies to be transferred closer to birth (*247*). Substantial active transport of maternal immunoglobulin G does not take place before 30 weeks of gestation (*255*). After receipt of Tdap, a minimum of 2 weeks is required to mount a maximal immune response to the vaccine antigens (*256*,*257*). One study noted that, after receipt of Tdap, maternal antibodies waned quickly; pregnant women who received Tdap during the first or second trimester had low levels of antibodies at term, suggesting that Tdap might need to be administered later in pregnancy to have high levels of antibodies for transfer to infants (*247*). Therefore, to optimize the concentration of vaccine-induced antipertussis antibodies transported from mother to infant, ACIP concluded in 2012 that pregnant women should be vaccinated with Tdap during the third trimester, preferably from 27 through 36 weeks' gestation (*6*).

New data available since 2012 suggest that vaccinating earlier in the 27 through 36-week time period will maximize passive antibody transfer to the infant (C. Mary Healy, Baylor College of Medicine, unpublished data, 2016) (*258–260*); however, it is unclear how this translates to effectiveness in preventing infant pertussis. Three studies have shown that, among infants whose mothers received Tdap during the 27 through 36 weeks' gestational time period, antipertussis antibody concentrations were significantly higher in cord blood of infants whose mothers received Tdap "earlier" (e.g., 27 through 32 weeks' gestation) compared with those who received Tdap "later" (e.g., after 32 weeks' gestation) (C. Mary Healy, Baylor College of Medicine, unpublished data, 2016) (*259*,*260*). A fourth study indicated that those who received Tdap as early as 22 through 26 weeks' gestation developed similar levels of antibody to those vaccinated 27 through 36 weeks' gestation (*258*). These studies support the observation that vaccinating earlier within the 27 through 36 week period, or even slightly before 27 weeks, might optimize the production and transfer of maternal antibodies to infants.

Assuring a sufficient amount of time between a pregnant woman's receipt of Tdap and her infant's birth to allow for the maximum production and transfer of maternal antibodies is important and might be achieved by vaccinating at a gestational age earlier than the current guidance of 27 through 36 weeks. However, ACIP is cautious not to equate higher newborn maternal antibody concentrations, which might be achieved through earlier maternal Tdap vaccination, with similar or better effectiveness at preventing pertussis during infancy.

Furthermore, it is unclear whether maternal vaccination earlier in pregnancy would result in the development and transfer of maternal antibodies at concentrations that would persist at protective levels until the infant's first DTaP dose. Lacking effectiveness data on vaccination before 27 weeks' gestation, ACIP concluded that vaccinating earlier in the 27 through 36 week period will maximize passive antibody transfer to the infant (*261*).

Vaccinating During Each Pregnancy

Studies of the persistence of antipertussis antibodies following a dose of Tdap show substantial decay in antibody levels after one year in healthy, nonpregnant adults (*186*,*262*,*263*); antibody kinetics in pregnant women are likely to be similar. With regard to maternal antipertussis antibody concentrations in infants born to women who received Tdap within the preceding 2 years, results from one study indicated that antipertussis antibody concentrations waned quickly in pregnant women vaccinated before pregnancy and were unlikely to be high enough to provide passive protection to infants (*247*). Because antibody levels wane substantially during the first year following vaccination, ACIP concluded that a single dose of Tdap during a pregnancy would be insufficient to provide protection for subsequent pregnancies (*6*).

Interference with Infant Immune Response to Primary Vaccination

The presence of maternally derived transplacental antipertussis antibodies might interfere with an infant's response to subsequent active vaccination with recommended DTaP vaccines potentially putting an infant at risk for disease later in infancy. In the United Kingdom, infants born to mothers who received Tdap-IPV during pregnancy had lower PT, FHA, and FIM antibodies when measured 3–6 weeks after the third dose of a 2-3-4 month schedule, compared with infants born to unvaccinated mothers (*264*). Antibodies to diphtheria also were lower, as were antibodies to some CRM-conjugated pneumococcal antigens when vaccinated with PCV13 on a 2–4-month schedule. In contrast, antitetanus antibody and anti-Hib antibody responses were enhanced. In the United States and Canada, pertussis antibody levels were modestly diminished (7.2%–48.3%) following the third dose of a 2-4-6 month DTaP schedule in infants whose mothers received Tdap during pregnancy, compared with infants whose mothers were not vaccinated during pregnancy; however, after the fourth dose of DTaP, pertussis antibody levels were comparable in the two groups of infants (S. A. Halperin, Dalhousie University, unpublished data, 2011) (*192*,*249*). Because correlates of protection are not well defined for pertussis, the clinical importance of lower infant immune responses following receipt of DTaP is unclear. However, any interference with infant immune responses is likely to be short-lived because circulating maternal antibodies decline rapidly (*265*). Although it is not known what level of maternal antibody is protective against infant pertussis, ACIP concluded that the potential benefit of protection from maternal antibodies in newborn infants outweighs the potential risk for shifting pertussis disease burden to later in infancy and emphasized the importance of timely receipt of the fourth DTaP dose (*9*).

"Cocooning"

ACIP recommends Tdap vaccination for women during pregnancy to prevent infant pertussis. Before this recommendation was developed to vaccinate pregnant women with Tdap, the primary strategy to prevent infant pertussis was Tdap vaccination of close contacts of infants, on the assumption that vaccination with Tdap would reduce the risk for pertussis exposure and transmission to infants, a strategy referred to as "cocooning" (*5*).

Cocooning programs had limited success and have been confronted with substantial logistical and financial challenges to implementation and program sustainability (*43*,*266*–*268*). Programs achieved moderate Tdap coverage among postpartum mothers, but had less success vaccinating other family members (*268*,*269*). The evidence on the effectiveness and impact of cocooning in preventing transmission of pertussis to infants is inconclusive (*153*,*154*,*270*). Recent epidemiologic and animal model evidence suggests that Tdap vaccination does not prevent transmission and therefore does not afford indirect protection of close contacts against pertussis (*155*,*156*,*159*). However, persons who are up to date with pertussis vaccines and who become infected generally have a milder infection compared with those who have not been vaccinated, which might make them less efficient in transmitting pertussis to others (*160*).

When recommendations for Tdap vaccination were made in 2005, mothers were identified as the primary source of pertussis in infants (*271*,*272*). This appears to have shifted, with siblings now identified as the primary source of pertussis infection for infants (*40*,*42*,*43*). This shift in the source of infant pertussis, along with recent evidence suggesting that Tdap vaccination does not prevent transmission of *B. pertussis*, underscores the importance of providing newborns with maternal antipertussis antibodies through Tdap vaccination of women during pregnancy (*155*,*156*,*159*). A single dose of Tdap is recommended for all persons aged ≥11 years who have not previously received a dose; having a pregnancy in a household presents an opportunity to review the Tdap vaccination status of close contacts to ensure that they are up to date.

Preventing Pertussis in Health Care Personnel

Health care personnel in the United States are not known to have higher risk for diphtheria or tetanus compared with the general population. However, for pertussis, occupational exposures occur in health care settings, and nosocomial spread of pertussis in various health care settings has been documented (*273–288*). In these settings, the index case might occur in a health care provider, patient, or hospital visitor (*273–288*). Although the frequency and intensity of patient exposure might lead to infection of health care personnel with subsequent transmission to other patients, the risk for and burden of pertussis in health care personnel are difficult to quantify. The few population-based estimates of the risk for pertussis among health care personnel in the United States suggest the risk for pertussis among health care personnel is comparable to the risk among the general population of adolescents and adults (*289–291*).

Since 2005, ACIP has recommended that health care personnel receive a single dose of Tdap to protect them against pertussis and possibly reduce transmission to patients, co-workers, household members, and persons in the community. Hospital-based Tdap coverage rates among health care personnel might depend on the type of Tdap vaccination program an institution employs; reported coverage ranges from 30% (campaign) to 100% (hospital mandate) (*292*,*293*). Nationally, Tdap coverage among health care personnel is 42.1% (*36*).

Previous models assessing the likely benefits and costs of vaccinating health care personnel with Tdap to prevent nosocomial pertussis outbreaks indicated that vaccination of health care personnel substantially reduced the risk for hospital-based outbreaks and was cost-saving (*294*,*295*). However, model inputs included estimates of Tdap vaccine efficacy against pertussis higher than current estimates, and assumed vaccination would decrease pertussis transmission and thereby prevent secondary cases. Current data do not support the assumption that Tdap vaccination would prevent transmission.

Management of Health Care Personnel Exposed to Pertussis

Depending on the approach used, management of pertussis exposures in health care settings can be complicated, time-consuming, and costly. Exposed health care personnel with cough illness must be evaluated and might require diagnostic testing, administration of prophylactic antimicrobial agents, and possible exclusion from work. Several studies have shown that the costs of investigating pertussis outbreaks in the health care setting and implementing control measures are substantial. The cost of managing pertussis exposures in the health care setting over a 12-month period ranged from $84,000 to $98,000 (*284*,*294*). The associated costs of dealing with hospital-based pertussis outbreaks ranged from $74,000 to $263,000 (*285*,*288*). Since the promulgation of the 2005 Tdap recommendations for health care personnel, only one study has tried to determine whether it is necessary to give Tdap-vaccinated health care personnel postexposure antimicrobial prophylaxis, but the results were inconclusive due to the low risk for disease during the study period (*296*).

Guidance on Postexposure Prophylaxis for Health Care Personnel

Tdap vaccination status does not change the approach to evaluating postexposure prophylaxis when health care personnel are exposed to pertussis. Postexposure prophylaxis is recommended for health care personnel in contact with persons at risk for severe disease (e.g., hospitalized neonates, newborn infants, and patients with chronic respiratory conditions). Other health care personnel can either receive postexposure prophylaxis or be carefully monitored for 21 days after pertussis exposure. Health care personnel should be treated with antibiotics at the onset of signs and symptoms of pertussis, and excluded from work for the first 5 days while receiving appropriate antibiotics. Recommended antimicrobial agents for postexposure prophylaxis among health care personnel exposed to pertussis include azithromycin, clarithromycin, erythromycin, and trimethoprim-sulfamethoxazole (TMP-SMX). Guidance on postexposure prophylaxis of pertussis is available at https://www.cdc.gov/mmwr/PDF/rr/rr5414.pdf.

No Additional Doses of Tdap for the General Population

With the exception of pregnant women, only a single booster dose of Tdap is recommended for persons aged ≥11 years. Both available Tdap products are approved for use as a single booster dose (*141*,*142*). Tdap provides protection against tetanus, diphtheria, and pertussis, but protection from pertussis infection begins to decline within 2 to 4 years after receipt of Tdap (*29*,*149*,*150*).

Clinical trials support that a second dose of Tdap is safe and immunogenic at a 5- or 10-year interval (*184–188*). Immunogenicity studies show that diphtheria and tetanus antibody levels persisted for five to 10 years after receipt of Tdap (*186*,*188*,*262*,*263*,*297–301*). However, antipertussis antibodies decline rapidly after the first year, suggesting that protection wanes, which would likely limit the impact of a second dose of Tdap on the overall burden of pertussis in the United States (*186*,*188*,*262*,*263*,*297–301*). Antibody decay and, therefore, clinical protection following additional doses

of Tdap are likely similar to what is observed following the first dose of Tdap.

ACIP recognizes the increasing burden of pertussis in the United States and the need for an effective strategy to reduce this burden. A decision analysis model evaluating the epidemiologic and economic impact of a routine program of additional doses of Tdap administered at either a 5- or 10-year interval to persons who received their first Tdap at age 11 years suggested that the reduction in pertussis disease burden attributable to the routine use of a second dose of Tdap would be limited (*302*). In the model, the proportion of cases preventable compared with the recommendation, ranged from 3% to 5% (*302*). ACIP concluded that the data do not support a general recommendation for a routine second dose of Tdap, and that the public health impact of routinely recommending a second dose of Tdap would be limited (*303*).

Rationale for Recommendations for Use of Pertussis, Tetanus, and Diphtheria Vaccines

Before the availability of vaccines, pertussis, tetanus, and diphtheria were common diseases and caused severe morbidity and mortality. As a result of the routine DTP/DTaP childhood vaccination program and decennial booster doses of tetanus-toxoid containing vaccines for adolescents and adults, the number of cases of all three diseases has declined markedly; cases of tetanus and diphtheria are rare in the United States. For pertussis, the number of reported cases declined dramatically following introduction of universal childhood pertussis vaccination (*3*). However, even with sustained high vaccine coverage, the incidence of reported pertussis began increasing in the 1980s.

In 1997, ACIP recommended that DTaP replace all DTP doses; since then, no changes have been made to these childhood vaccine recommendations (*3*). In 2005, to address the increase in the incidence of pertussis among adolescents and adults, ACIP recommended a single dose of Tdap for persons aged 11–64 years as a booster immunization against tetanus, diphtheria, and pertussis, with the intention to provide routine vaccination at ages 11–12 years (*4*,*5*). Additionally, special populations, including health care personnel and close contacts of infants, were recommended to receive a dose of Tdap.

Since the promulgation of the ACIP Tdap recommendations in 2005, several studies have identified barriers to and programmatic gaps in the implementation of the recommendations for adolescents and adults. Barriers to implementation included confusion around guidance language concerning the timing of administration of Tdap after the last tetanus toxoid–containing vaccine dose and obstacles to vaccinating health care personnel. Programmatic gaps at the time of the 2005 recommendations included lack of a Tdap vaccine licensed for children aged 7–10 years and for adults aged ≥65 years. In 2011 and 2012, ACIP recommended a dose of Tdap for these age groups and clarified the language concerning the timing of Tdap vaccination and the vaccination of health care personnel (*8*,*10*,*304*).

Compared with older children and adults, infants aged <12 months have substantially higher rates of pertussis (Figure 2) and the largest burden of pertussis-related deaths. The majority of pertussis-related hospitalizations and deaths occur in infants aged ≤2 months who are too young to be vaccinated. The desire to protect the youngest infants from pertussis morbidity and mortality prompted ACIP in 2011 to recommend a dose of Tdap be administered to women during pregnancy, but only for pregnant women who had never received Tdap (*9*). Because antibody levels wane substantially after vaccination, ACIP concluded that a single dose of Tdap during one pregnancy would not provide protection for infants who were the product of subsequent pregnancies. In 2012, the recommendation was revised; ACIP recommends the use of Tdap during each pregnancy (*6*).

Recommendations for Vaccination for Pertussis, Tetanus, and Diphtheria

All persons are recommended to receive routine pertussis, tetanus, and diphtheria vaccination. Vaccine type, product, number of doses and booster dose recommendations are based on age and pregnancy status (Tables 4 and 5). Recommendations for off-label use of Tdap vaccines were made after thorough review of available data on the risks for and benefits of Tdap vaccination, and include the following persons: pregnant women, children aged 7–10 years, and persons aged ≥65 years (for one Tdap product) (*6*,*8*–*10*). At the time these recommendations were made, ACIP determined that although data were limited, the benefits of off-label Tdap vaccination in preventing pertussis and decreasing pertussis-related morbidity and mortality outweigh the risks of an adverse event.

General Recommendations

Persons Aged 2 Months–6 Years

The routine pertussis, tetanus, and diphtheria vaccination schedule for persons aged 2 months–6 years is comprised of five doses of vaccine containing diphtheria and tetanus toxoids, and pertussis antigens (DTaP), administered at ages 2, 4, 6, 15–18 months and 4–6 years.

- Three (primary) doses should be administered at ages 2, 4, and 6 months.
- The fourth (first booster) dose should be administered to children aged 15–18 months to maintain adequate immunity during preschool years.
- The fifth (second booster) dose should be administered to children aged 4–6 years to confer continued protection against disease during the early years of schooling.

Guidance for Use

The first DTaP dose can be administered as early as age 6 weeks.

The fourth DTaP dose should be administered at least 6 months after the third DTaP dose and should not be administered to a child aged <12 months.

A fifth DTaP dose is not necessary if the fourth DTaP dose in the series is administered at age ≥4 years.

Persons Aged 11–18 Years

Persons aged 11–18 years should receive a single dose of Tdap, preferably at a preventive care visit at ages 11–12 years. To ensure continued protection against tetanus and diphtheria, booster doses of Td should be administered every 10 years throughout life.

Persons Aged ≥19 Years

Persons aged ≥19 years who previously have not received a dose of Tdap should receive a single dose of Tdap in place of a decennial Td booster dose. The dose of Tdap, when indicated, should not be delayed and should be administered regardless of interval since the last tetanus or diphtheria toxoid–containing vaccine. To ensure continued protection against tetanus and diphtheria, booster doses of Td should be administered every 10 years throughout life.

Pregnant Women

ACIP recommends that providers of prenatal care implement a Tdap immunization program for all pregnant women. Health care personnel should administer a dose of Tdap during each pregnancy, irrespective of the patient's prior history of receiving the vaccine.

Guidance for Use

Tdap should be administered between 27 and 36 weeks' gestation, although it may be administered at any time during pregnancy. Available data suggest that vaccinating earlier in the 27–36 week time period will maximize passive antibody transfer to the infant.

Tdap may be simultaneously administered with an inactivated influenza vaccine to pregnant women.

If a woman did not receive Tdap during her current pregnancy and did not receive a prior dose of Tdap ever (i.e., during adolescence, adulthood, or a previous pregnancy), then Tdap should be administered immediately postpartum. If a woman did not receive Tdap during her current pregnancy but did receive a prior dose of Tdap, then she should not receive a dose of Tdap postpartum.

Vaccination of Special Populations

Persons Aged 2 Months–6 Years

Contraindications to pertussis vaccination. For children aged <7 years with a contraindication to pertussis vaccination (Table 2), DT should be used instead of DTaP to complete an age appropriate series. Previously unvaccinated children who receive their first DT dose at age <12 months should receive a total of 4 doses of DT, the first 3 doses at 4- to 8-week intervals and the fourth dose 6 to 12 months later (similar to the recommended DTaP schedule).

Unvaccinated children aged ≥12 months for whom pertussis vaccine is contraindicated should receive 2 doses of DT 4 to 8 weeks apart, followed by a third dose 6 to 12 months later to complete the primary series. Children who have already received 1 or 2 doses of DT or DTaP after their first birthday and for whom further pertussis vaccine is contraindicated should receive a total of 3 doses of a preparation containing diphtheria and tetanus toxoids appropriate for age, with the third dose administered 6 to 12 months after the second dose.

Children aged 4–6 years who complete a primary series of DT before their fourth birthday should receive a fifth dose of DT by the time of school entry to confer continued protection against disease.

Personal history of seizures. Among infants and children with a history of previous seizures, it is prudent to delay pertussis vaccination until the child's neurologic status has been assessed. Infants and children with a stable neurologic condition, including well-controlled seizures, may be vaccinated with DTaP. Infants with evolving neurologic conditions should not be vaccinated until a treatment regimen has been established and the condition has stabilized. A family history of seizures is not a contradiction to pertussis vaccination.

Persons Aged ≥11 Years

Close contacts of infants. Persons aged ≥11 years who have or anticipate having close contact with an infant aged ≤12 months (e.g., parents, siblings, grandparents, child care providers, and health care providers) and who have never received Tdap should receive a dose of Tdap. Ideally, these persons should receive Tdap at least 2 weeks prior to contact with the infant to allow for an immune response to pertussis vaccine antigens.

Health care personnel. All health care personnel should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap. After receipt of 1 dose of Tdap, health care personnel should receive routine Td booster immunizations according to the recommended schedule.

In-patient and out-patient care facilities should consider approaches that maximize vaccination rates of health care personnel (e.g., education about the benefits of vaccination, convenient access, provision of Tdap at no charge).

Persons with Incomplete or Unknown Vaccine History

Persons Aged 2 Months–6 Years

For persons aged <7 years not fully immunized with DTaP vaccine, the catch-up schedule and minimum intervals between doses are available at https://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html. The vaccine series does not need to be restarted regardless of the time that has elapsed between doses for those with incomplete DTaP vaccine history.

Because of concern about adverse reactions, the total number of doses of vaccines containing diphtheria and tetanus toxoids (e.g., DTaP, DT, and DTP) received should not exceed 6 doses before the seventh birthday. Only documented doses count toward the maximum of 6 doses.

Persons Aged 7–18 Years

Persons aged 7–18 years not fully immunized with DTaP vaccine should receive a single dose of Tdap as one (preferably the first) dose of the catch-up series; if additional doses are needed, use Td vaccine. The vaccine series does not need to be restarted, regardless of the time that has elapsed between doses for those with incomplete DTaP vaccine history. The catch-up schedule and minimum intervals between doses are available at https://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html.

For persons aged 7–10 years who receive a dose of Tdap as part of the catch-up series, an adolescent Tdap vaccine dose should be administered at age 11–12 years.

Persons Aged >18 Years

Persons aged >18 years who have never been vaccinated against pertussis, tetanus, or diphtheria should receive a series of three vaccinations containing tetanus and diphtheria toxoids, which includes 1 dose of Tdap. The preferred schedule is a single dose of Tdap, followed by a dose of Td at least 4 weeks after Tdap and another dose of Td 6 to 12 months later. However, the single dose of Tdap can substitute for any of the Td doses in the 3-dose primary series.

Persons aged >18 years who are not fully immunized against tetanus and diphtheria should receive 1 dose of Tdap (preferably the first) in the catch-up series; if additional tetanus toxoid–containing doses are needed, use Td vaccine. Alternatively, in situations in which a person aged >18 years probably received vaccination against tetanus and diphtheria but cannot produce documentation, vaccine providers may consider serologic testing for antibodies to tetanus and diphtheria toxin to avoid unnecessary vaccination. If tetanus and diphtheria antitoxin levels are each >0.01 IU/mL, previous vaccination with tetanus and diphtheria toxoid vaccine is presumed, and a single dose of Tdap is indicated.

Prevention of Obstetric and Neonatal Tetanus

Pregnant women who have completed the childhood immunization schedule and were last vaccinated more than ten years previously should receive a booster dose of tetanus toxoid–containing vaccine to prevent neonatal tetanus. The risk of neonatal tetanus is minimal if a previously unimmunized woman has received at least 2 properly spaced doses of tetanus toxoid–containing vaccine during pregnancy; one of the doses administered during pregnancy should be Tdap, administered according to the current guidance. She should complete the 3-dose primary series at the recommended intervals.

Tetanus Prophylaxis for Wound Management

ACIP has recommended administering tetanus toxoid–containing vaccine and tetanus immune globulin (TIG) when indicated as part of standard wound management to prevent tetanus (Table 6). A tetanus toxoid–containing vaccine is indicated as part of wound management if more than five years has passed since the last tetanus toxoid–containing vaccine dose. If a tetanus toxoid–containing vaccine is indicated for persons aged ≥11 years, Tdap is preferred for persons who have not previously received Tdap or whose Tdap history is unknown. If a tetanus toxoid–containing vaccine is indicated for a pregnant woman, Tdap should be used. For nonpregnant persons with documentation of previous vaccination with Tdap, Td should be used if a tetanus toxoid–containing vaccine is indicated. If a tetanus toxoid–containing vaccine is indicated and Td is unavailable, Tdap may be administered.

Persons who have completed the 3-dose primary tetanus vaccination series and have received a tetanus toxoid–containing vaccine <5 years earlier are protected against tetanus and do not require a tetanus toxoid–containing vaccine or TIG as part of wound management. An attempt should be made to determine

TABLE 6. Guide to tetanus prophylaxis in routine wound management

No. doses of adsorbed tetanus toxoid–containing vaccines	Clean and minor wound		All other wounds*	
	DTaP, Tdap, or Td†	TIG	DTaP, Tdap, or Td†	TIG§
Unknown or <3	Yes	No	Yes	Yes
≥3	No¶	No	No**	No

Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td = tetanus and diphtheria toxoids; TIG = tetanus immune globulin.

* Such as, but not limited to, wounds contaminated with dirt, feces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.

† DTaP is recommended for children aged <7 years. Tdap is preferred to Td for persons aged ≥11 years who have not previously received Tdap. Persons aged ≥7 years who are not fully immunized against pertussis, tetanus or diphtheria should receive one dose of Tdap for wound management and as part of the catch-up series.

§ Persons with HIV infection or severe immunodeficiency who have contaminated wounds should also receive TIG, regardless of their history of tetanus immunization.

¶ Yes, if ≥10 years since the last tetanus toxoid–containing vaccine dose.

** Yes, if ≥5 years since the last tetanus toxoid–containing vaccine dose.

whether a patient has completed the 3-dose primary tetanus vaccination series. Persons with unknown or uncertain previous tetanus vaccination histories should be considered to have had no previous tetanus toxoid–containing vaccine. Persons who have not completed the primary series might require tetanus toxoid–containing vaccine and passive vaccination with TIG at the time of wound management (Table 6). When both TIG and a tetanus toxoid–containing vaccine are indicated, the products should be administered using separate syringes at different anatomical sites. Persons with human immunodeficiency virus (HIV) infection or severe immunodeficiency who have contaminated wounds should also receive TIG, regardless of their history of tetanus immunizations.

Persons with a history of an Arthus reaction following a previous dose of a tetanus toxoid–containing vaccine should not receive a tetanus toxoid–containing vaccine until >10 years after the most recent dose; this interval is recommended regardless of the wound condition (e.g., even if contaminated or severe). In all circumstances, the decision to administer TIG should be based on the primary vaccination history for tetanus (Table 6).

Special Situations

Accelerated Schedule for Infants and Children Aged <7 Years

For an infant or child aged <7 years, circumstances such as travel, potential loss to follow-up or increased risk of exposure to pertussis might warrant an accelerated schedule to provide protection as early as possible. An accelerated schedule can be started as soon as the infant is aged 6 weeks, with the second and third DTaP doses administered no earlier than 4 weeks after each preceding dose. The fourth DTaP dose should not be administered before the infant is aged 12 months and should be separated from the third dose by at least 6 months. The fifth DTaP dose should not be administered before the child is aged 4 years. When considering an accelerated schedule, providers also should consider the timing of other recommended vaccines and well-child visits.

History of Pertussis

Persons who have a history of pertussis should receive a pertussis-containing vaccine (i.e., DTaP or Tdap) according to the routine recommendation. Although pertussis disease is likely to confer natural immunity against pertussis, the immune response might be suboptimal against subsequent pertussis disease and the duration of protection induced by an infection does not provide long-term immunity (*305*,*306*).

Persons Who Have Recovered from Tetanus or Diphtheria

Tetanus or diphtheria infection do not necessarily confer immunity against re-infection (*54*,*307*,*308*); therefore, active vaccination should be initiated at the time of recovery from the illness according to the schedule. Persons who have completed the primary tetanus vaccination series should receive a booster dose as soon as feasible during convalescence. Persons with unknown or uncertain previous tetanus vaccination histories should be considered to have had no previous tetanus toxoid–containing vaccine and should begin the 3-dose tetanus and diphtheria toxoids vaccination series.

Vaccine Administration

A summary of dose schedules is provided (Tables 4 and 5).

All health care personnel administering vaccinations should be aware of the potential for syncope after vaccination, especially among adolescents and young adults, and should take appropriate measures to prevent potential injuries. Providers should strongly consider observing patients for 15 minutes after they are vaccinated. If syncope occurs, the vaccine recipient should be observed until symptoms resolve (*52*).

DTaP

Six vaccines are licensed for the pertussis, tetanus and diphtheria vaccination series (Table 4). The dose of DTaP is 0.5 mL, administered intramuscularly. The preferred intramuscular injection site for infants and children through age 2 years is the anterolateral aspect of the thigh (*52*). For children aged ≥3 years, the preferred site is the deltoid muscle

(*52*). DTaP may be administered simultaneously with other vaccines at a different anatomical site.

Interchangeable use of acellular pertussis vaccines. Whenever feasible, the same DTaP product should be used for all doses of the vaccination series. Data are limited regarding the safety, immunogenicity, and efficacy of using DTaP vaccines from different manufacturers for successive doses of the primary or booster vaccination series. However, the vaccine provider might not know or have available the type of DTaP vaccine previously administered to a child; neither circumstance should present a barrier to administration of the vaccine. Any of the licensed DTaP vaccines may be used to complete the vaccination series.

Minimum interval between third and fourth DTaP dose. The recommended minimal interval between the third and fourth doses of DTaP is 6 months, and the minimum age for receipt of the fourth dose of DTaP is 12 months. However, a fourth DTaP dose is considered valid if administered at least 4 months after the third dose of DTaP and the child is aged ≥12 months.

DT

One vaccine is licensed for active immunization of children up to age seven years against diphtheria and tetanus in instances where the pertussis vaccine component is contraindicated or where the physician decides that pertussis vaccine is not to be administered (Table 4). The dose of DT is 0.5 mL, administered intramuscularly. The preferred intramuscular injection site for infants and children through age 2 years is the anterolateral aspect of the thigh (*52*). For children aged ≥3 years, the preferred site is the deltoid muscle (*52*).

Tdap

Two vaccines are licensed for the pertussis, tetanus and diphtheria vaccination booster dose for adolescents and adults (Table 5). The dose of Tdap is 0.5 mL, administered intramuscularly, preferably into the deltoid muscle (*52*). Tdap may be administered simultaneously with other vaccines at a different anatomical site.

Interval between Td and Tdap. ACIP recommends that for pertussis vaccination, when indicated, Tdap should be administered regardless of interval since the last tetanus or diphtheria toxoid–containing vaccine. ACIP concluded that, while longer intervals between Td and Tdap vaccination could decrease the occurrence of local reactions, the benefits of protection against pertussis outweigh the potential risk for adverse events. For persons aged ≥7 years with incomplete or unknown vaccine history, the interval between doses of tetanus toxoid–containing vaccines should follow the catch-up series schedule.

Tdap products in adults aged ≥65 years. Providers should not miss an opportunity to vaccinate persons aged ≥65 years with Tdap. When feasible, Boostrix (approved for use in persons aged ≥10 years) should be used for adults aged ≥65 years instead of Adacel (approved for use in persons aged 10–64 years); however, ACIP concluded that either vaccine administered to a person aged ≥65 years is immunogenic and would provide protection. A dose of either Tdap product is considered valid; therefore, providers may administer the Tdap vaccine they have available.

Td

For tetanus and diphtheria toxoids adsorbed vaccines, there are two licensed vaccines (Table 5). The dose of Td is 0.5 mL, administered intramuscularly, preferably into the deltoid muscle (*52*).

Inadvertent Administration

DTaP

DTaP is not indicated for persons aged ≥7 years. If DTaP is administered inadvertently to a fully vaccinated child aged 7–10 years, this dose should be counted as the adolescent Tdap dose. If DTaP is administered inadvertently to an undervaccinated child aged 7–10 years, this dose should count as the Tdap dose of the catch-up series and the child should receive an adolescent booster dose of Tdap. If DTaP is administered inadvertently to a person aged ≥11 years, this dose should count as the Tdap dose, and the person should not receive an additional dose of Tdap.

Tdap

Persons aged 2 months–6 years. If Tdap is administered inadvertently instead of DTaP as any one of the first 3 doses of the tetanus-diphtheria-pertussis vaccination series, the Tdap dose should not be counted as valid, and a replacement dose of DTaP should be administered. The replacement dose of DTaP can be administered as soon as feasible at any interval after the inadvertent Tdap dose. The remaining doses of the DTaP series should be administered on the routine schedule, with at least a four-week interval between the replacement dose of DTaP and the next dose of DTaP. The adolescent Tdap dose should be administered as recommended when this child is aged 11–12 years.

If Tdap is administered inadvertently as the fourth or the fifth dose in the tetanus-diphtheria-pertussis vaccination series, the Tdap dose should be counted as valid and does not need to be repeated; the child who received Tdap as a fourth dose should complete the pediatric DTaP schedule. The adolescent

Tdap dose should be administered as recommended when this child is aged 11–12 years.

Children aged 7–10 years who are fully vaccinated.[¶] If Tdap is administered inadvertently, the Tdap dose should not be counted as valid. The adolescent Tdap dose should be administered as recommended when this child is aged 11–12 years.

Additional Doses of Tdap for the General Population

Both Tdap products are licensed for use as a single dose for active booster immunization; Boostrix is approved for use in persons aged ≥10 years and Adacel is approved for use in persons aged 10–64 years. Tdap is not licensed for multiple administrations nor is it recommended for multiple administrations, with the exception of the recommendation that pregnant women receive a dose of Tdap during each pregnancy. If a dose of Tdap is administered to a person who has previously received Tdap, this dose should count as the next booster dose of tetanus toxoid–containing vaccine.

Contraindications and Precautions

Providers should screen patients for contraindications and precautions to the vaccine before each dose of vaccine is administered (Table 2). A contraindication is a condition in a recipient that increases the risk for a serious adverse reaction. A vaccine should not be administered when a contraindication is present. In contrast, certain conditions are commonly misperceived as contraindications (i.e., are not valid reasons to defer vaccination) (Table 3). In general, vaccinations should be deferred when a precaution is present. However, a vaccination might be indicated in the presence of a precaution if the perceived benefit of protection from the vaccine outweighs the risk for an adverse reaction.

For DTaP vaccines, providers and parents should evaluate the risks and benefits of administering subsequent doses of a pertussis-containing vaccine. In circumstances in which the benefits of further pertussis vaccination outweigh the possible risks (e.g., during an outbreak of pertussis), DTaP vaccine should be administered for the subsequent doses.

Reporting of Vaccine Adverse Events

Clinically significant and serious adverse events that arise after vaccination should be reported to VAERS at https://vaers.hhs.gov/reportevent.html. VAERS is a postmarketing safety surveillance program that collects information about adverse events (possible side effects) that occur after the administration of vaccines licensed for use in the United States.

Reports can be filed securely online, by mail, or by fax. A VAERS form can be downloaded from the VAERS website or requested by e-mail (info@vaers.org), telephone (800-822-7967), or fax (877-721-0366). Additional information on VAERS and vaccine safety is available at https://vaers.hhs.gov/about/index or by calling telephone 800-822-7967.

National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program (VICP), established by the National Childhood Vaccine Injury Act of 1986, as amended, provides a mechanism through which compensation can be paid on behalf of a person determined to have been injured or to have died as a result of receiving a vaccine covered by VICP. National Childhood Vaccine Injury Act requires health care providers to report any adverse events listed by the manufacturer as a contraindication to further vaccination or any adverse event listed in the VAERS Table of Reportable Events Following Vaccination that occurs within the specified time period after vaccination. The Vaccine Injury Table lists the vaccines covered by VICP and the injuries and conditions (including death) for which compensation might be paid. If the injury or condition is not included in the table or does not occur within the time period specified on the table, persons must prove that the vaccine caused the injury or condition. For a person to be eligible for compensation, the general filing deadlines for injuries require claims to be filed within 3 years after the first sign or symptom of the vaccine injury; for a death, claims must be filed within 2 years of the vaccine-related death and not more than 4 years after the start of the first sign or symptom of the vaccine-related injury from which the death occurred. When a new vaccine is covered by VICP or when a new injury/condition is added to the table, claims that do not meet the general filing deadlines must be filed within 2 years from the date the vaccine or injury/condition is added to the table for injuries or deaths that occurred up to 8 years before the table change. Persons who receive a VICP-covered vaccine might be eligible to file a claim. Additional information about VICP is available https://www.hrsa.gov/vaccinecompensation/index.html or by calling 800–338–2382.

[¶] Fully vaccinated is defined as having received 5 valid doses of DTaP or 4 valid doses of DTaP if the fourth dose was administered on or after the fourth birthday.

Safety Monitoring in Pregnant Women

Safety monitoring in pregnant women following Tdap administration includes enhanced monitoring in VAERS and utilization of the VSD to assess acute adverse events during pregnancy, adverse pregnancy outcomes affecting the mother, and birth outcomes.

Although not required by the FDA, pregnancy registries were established by Sanofi Pasteur and GSK during licensure of both Tdap vaccines to collect data on adverse events following inadvertent administration of Tdap vaccine during pregnancy. ACIP recommends administration of Tdap vaccine during each pregnancy. Neither Tdap product is contraindicated for use in pregnant women; lack of a specific "indication and usage" statement about use of the product in pregnant women in the product labeling does not preclude use of these vaccines during pregnancy. Both pharmaceutical companies continue to maintain a pregnancy registry. Health care providers may report Tdap vaccination during pregnancy, regardless of trimester, to the appropriate company's pregnancy registry: Sanofi Pasteur (Adacel) telephone: 800-822-2463 and GSK (Boostrix) telephone: 888-452-9622.

Future Directions

The United States has experienced substantial increases in the number of reported pertussis cases and changes in the epidemiologic features of pertussis since the early 1990s. The impact of switching from whole-cell pertussis vaccines (DTP) to acellular pertussis vaccines (DTaP) on the epidemiologic features of pertussis is still being investigated. Both DTaP and Tdap vaccines remain the most effective tools for preventing pertussis disease and are associated with fewer serious adverse events than DTP, but data thus far indicate that they do not provide long-term protection and might not prevent transmission.

Since the introduction of a single Tdap booster vaccine for adolescents and adults in 2005, changes to the recommendation were made in order to reduce barriers to Tdap uptake and coverage among adolescents and adults and to reduce the burden of pertussis in infants. High vaccine coverage in adolescents is being achieved and has met the *Healthy People 2020* target (80%), but attaining high coverage among adults remains a challenge (*35*). Despite challenges to vaccinating women during pregnancy, focused efforts to educate providers and pregnant women have resulted in gradual improvement in Tdap coverage. Ongoing efforts are needed to increase Tdap coverage in each pregnancy to optimize prevention of severe pertussis in young infants. The effects of the changes made to the Tdap recommendations need to be monitored and evaluated over time for their effectiveness and impact on pertussis, particularly in infants.

As the epidemiologic features of pertussis in the United States continue to evolve and more is understood about acellular pertussis vaccines, reassessment of immunization strategies might be required in the future. Looking ahead, the ability to improve the current prevention and control strategies is limited by gaps in the understanding of the immune response to acellular pertussis vaccines and pertussis infection, as well as the lack of accepted defined serologic or laboratory correlates of protection against pertussis. Given existing understanding of the durability of protection provided by the current pertussis vaccines, optimizing the current pertussis vaccination program and protecting infants, who are at highest risk for pertussis-related death, are immediate priorities.

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Disclosure of Relationship

CDC planners and content experts wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters. This report includes discussion of the unlabeled use of diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccines or tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine in the following situations:

1. The following conditions are considered precautions and not contraindications as indicated in DTaP package inserts: progressive neurologic disorders including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy.
2. The administration of the fourth dose of DTaP may be at an age younger than the approved age indicated in the package insert.
3. The minimum interval between the last tetanus toxoid–containing vaccine and receipt of Tdap may be shorter than the 5 years indicated in the package insert.
4. The administration of Tdap may be at an age younger than the approved age indicated in the package insert.
5. The administration of Tdap as part of the catch-up series for tetanus and diphtheria for persons aged >18 years.
6. The administration of Tdap is recommended for women during pregnancy.
7. The administration of Adacel (Tdap, Sanofi Pasteur, Swiftwater, Pennsylvania) may be at an age older than the approved age indicated in the package insert.
8. The inadvertent administration of DTaP at an age older than the approved age indicated in the package insert.
9. The inadvertent administration of Tdap at an age younger than the approved age indicated in the package insert.

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From:	Nair, Narayan (HRSA)
To:	Atanasoff, Sarah (HRSA); Dalle-Tezze, Terry (HRSA); Ditmar, Mark (HRSA); Luna, Kenneth (HRSA); Melo, Marco (HRSA); Osborn, Mark (HRSA); Rubin, Mary (HRSA); Sisk, Nasrin (HRSA); St. Martin, Laura (HRSA); Stryer, Stacy (HRSA)
Subject:	FW: ACIP updates
Date:	Thursday, March 22, 2018 3:56:11 PM
Attachments:	ltr-mbr-candidates.pdf

Good morning, please see the attachment and email below from the ACIP. There are looking for new members. This is an opportunity for **NON-FEDERAL** individuals to serve and share their expertise. Feel free to circulate if you know anyone suitable.

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From: MacNeil, Jessica R. (CDC/OID/NCIRD) [mailto:aji8@cdc.gov]
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Cc: Cohn, Amanda (CDC/OID/NCIRD) <anc0@CDC.GOV>; Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Subject: ACIP updates

Hello everyone,

Thanks again for your participation in the February ACIP meeting! Attached is an ACIP Dashboard with updates from the February meeting, a summary of the ACIP Secretariat's current activities and priorities, and a summary of each of the Work Group's ongoing activities.

We are currently in the process of trying to identify exceptional candidates for the next group of ACIP voting members. In particular, this year we are hoping to identify candidates with expertise in either **adult medicine or nursing, as well as female and minority applicants**. If you know someone who would make a good ACIP voting member **please encourage him or her to apply**, or let us know and we will reach out to him or her! More information on the nomination process is included in the attached letter.

As always, please don't hesitate to reach out to either Amanda, or myself, if you have any questions, concerns, or suggestions!

Best regards,

Jessica

Jessica MacNeil, MPH
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DATE: January 2018

FROM: Executive Secretary, ACIP

SUBJECT: Nomination of Candidates for the Advisory Committee on Immunization Practices (ACIP)

The period for solicitation of potential nominees to replace the ACIP members whose terms will end on June 30, 2018 has concluded. We are now accepting applications for membership for the term beginning July 1, 2019; we will be filling four positions at that time.

We are happy to receive proposals at any time of the year for candidates to fill upcoming vacancies on the Advisory Committee on Immunization Practices (ACIP). Selection of members is based on candidates' qualifications to contribute to the accomplishment of ACIP objectives (www.cdc.gov/vaccines/acip/index.html). The U.S. Department of Health and Human Services policy stipulates that committee membership be balanced in terms of professional training and background, points of view represented, and the committee's function. Consideration is given to a broad representation of geographic areas within the U.S., with equitable representation of the sexes, ethnic and racial minorities, and the handicapped. Nominees must be U.S. citizens, and cannot be full- time employees of the U.S. Government.

Candidates should submit the following items:

- Current ***curriculum vitae***, **including complete contact information** (telephone numbers, mailing address, e-mail address)
- At least one letter of recommendation **from person(s) not employed by the U.S. Department of Health and Human Services**
    - One letter should be written by someone at your institution who is familiar with your current work.
    - More than one letter may be submitted.
- A cover letter that includes your statement of interest in serving on the ACIP, the qualifications and expertise that you would bring, and written evidence to support how you meet all of the relevant criteria, which are identified in the "Qualities required for ACIP Members" section included in *Detailed Information regarding ACIP Membership.*

The deadline for receipt of all application materials is **August 1, 2018**. **All files must be submitted electronically as e-mail attachments to:**

Ms. Stephanie Thomas
c/o ACIP Secretariat
e-mail: SThomas5@cdc.gov

Nominations may be submitted by the candidate him- or herself, or by the person/organization recommending the candidate.

A review of all applications will be conducted in the fall of 2018 by the ACIP Steering Committee, with final selection of the candidates to be made by the Secretary, Department of Health and Human Services; successful candidates will be notified of their appointment during the spring of 2019 and those candidates not accepted will be informed in writing. Unsuccessful applicants are encouraged to re-apply

in subsequent years. The need for various kinds of expertise varies from year to year and a candidate who is not selected in one year may be appointed in a subsequent year.

If you have any questions regarding these procedures, please email Ms. Stephanie Thomas at SThomas5@cdc.gov.

Please share this request with anyone who may be interested in submitting a recommendation for nomination.

Amanda Cohn, MD
Executive Secretary

From: Nair, Narayan (HRSA)
To: Thomas, Stephanie B. (CDC/DDID/NCIRD/OD); MacNeil, Jessica R. (CDC/DDID/NCIRD/OD)
Cc: Cohn, Amanda (CDC/DDID/NCIRD/OD); Rubin, Mary (HRSA)
Subject: RE: ACIP updates
Date: Wednesday, March 21, 2018 3:29:24 PM

OK, thanks for the info.

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Cc: Cohn, Amanda (CDC/OID/NCIRD) <anc0@CDC.GOV>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: ACIP updates

Thanks Narayan!

Please register for the meeting and at the meeting you will have a seat at the table, near the podium at the tables around the outside of the voting members.

https://www2a.cdc.gov/vaccines/acip/juneregistration.asp

Stephanie

From: Nair, Narayan (HRSA)
Sent: Wednesday, March 21, 2018 3:19 PM
To: MacNeil, Jessica R. (CDC/OID/NCIRD) <aji8@cdc.gov>; MacNeil, Jessica R. (CDC/OID/NCIRD) <aji8@cdc.gov>
Cc: Cohn, Amanda (CDC/OID/NCIRD) <anc0@cdc.gov>; Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: ACIP updates

Good afternoon Jessica,

FYI - I have a conflict for the June ACIP meeting so Dr. Mary Rubin, a pediatrician who has been with VICP for many years, will be attending in my place. She is extremely knowledgeable about the program and I believe this will be her first visit to CDC. Let us know if there is anyone else I should notify to get her set up to attend the meeting.

Narayan Nair, MD
CAPT, USPHS
Division Director/Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau

Health Resources and Services Administration
5600 Fishers Lane, Room 8N23
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Telephone: 301-443–5287
Fax: 301-443-0704
E-mail: nnair@hrsa.gov

From: MacNeil, Jessica R. (CDC/OID/NCIRD) [mailto:aji8@cdc.gov]
Sent: Tuesday, March 20, 2018 3:22 PM
To: MacNeil, Jessica R. (CDC/OID/NCIRD) <aji8@CDC.GOV>
Cc: Cohn, Amanda (CDC/OID/NCIRD) <anc0@CDC.GOV>; Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>
Subject: ACIP updates

Hello everyone,

Thanks again for your participation in the February ACIP meeting! Attached is an ACIP Dashboard with updates from the February meeting, a summary of the ACIP Secretariat's current activities and priorities, and a summary of each of the Work Group's ongoing activities.

We are currently in the process of trying to identify exceptional candidates for the next group of ACIP voting members. In particular, this year we are hoping to identify candidates with expertise in either **adult medicine or nursing, as well as female and minority applicants**. If you know someone who would make a good ACIP voting member **please encourage him or her to apply**, or let us know and we will reach out to him or her! More information on the nomination process is included in the attached letter.

As always, please don't hesitate to reach out to either Amanda, or myself, if you have any questions, concerns, or suggestions!

Best regards,
Jessica

Jessica MacNeil, MPH
Epidemiologist
Deputy Executive Secretary, Advisory Committee on Immunization Practices
Centers for Disease Control and Prevention
1600 Clifton Road NE, MS C-25
Atlanta, GA 30329-4027
Phone: (404) 639-1194
Cell: (b) (6)
Fax: (404) 315-4681
Email: jmacneil@cdc.gov

From: Nair, Narayan (HRSA)
To: Rubin, Mary (HRSA)
Subject: RE: ACIP updates
Date: Wednesday, March 21, 2018 3:35:10 PM

Correct
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From: Rubin, Mary (HRSA)
Sent: Wednesday, March 21, 2018 3:35 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: ACIP updates

And your office address not your home address, right?

From: Nair, Narayan (HRSA)
Sent: Wednesday, March 21, 2018 3:33 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: ACIP updates

You can put HRSA. I think that is what I put.
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E-mail: nnair@hrsa.gov

From: Rubin, Mary (HRSA)
Sent: Wednesday, March 21, 2018 3:32 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: ACIP updates

In seriousness, do I put Division of Injury Compensation Programs or HRSA (spelled out) for organization

---

From: Nair, Narayan (HRSA)

Sent: Wednesday, March 21, 2018 3:30 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: FW: ACIP updates

Please register for the meeting at the site below. Let me know if you need help with the math problem.

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From: Thomas, Stephanie B. (CDC/OID/NCIRD) [mailto:hkp4@cdc.gov]
Sent: Wednesday, March 21, 2018 3:23 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>; MacNeil, Jessica R. (CDC/OID/NCIRD) <aji8@CDC.GOV>
Cc: Cohn, Amanda (CDC/OID/NCIRD) <anc0@CDC.GOV>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: ACIP updates

Thanks Narayan!
Please register for the meeting and at the meeting you will have a seat at the table, near the podium at the tables around the outside of the voting members.
https://www2a.cdc.gov/vaccines/acip/juneregistration.asp
Stephanie

From: Nair, Narayan (HRSA)
Sent: Wednesday, March 21, 2018 3:19 PM
To: MacNeil, Jessica R. (CDC/OID/NCIRD) <aji8@cdc.gov>; MacNeil, Jessica R. (CDC/OID/NCIRD) <aji8@cdc.gov>
Cc: Cohn, Amanda (CDC/OID/NCIRD) <anc0@cdc.gov>; Thomas, Stephanie B. (CDC/OID/NCIRD) <hkp4@cdc.gov>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: ACIP updates

Good afternoon Jessica,
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Best regards,
Jessica

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Email: jmacneil@cdc.gov

From: Nair, Narayan (HRSA)
To: Rubin, Mary (HRSA)
Subject: RE: Free trip to Atlanta!
Date: Monday, March 19, 2018 10:51:32 AM

Usually a month or so before the meeting they send out the notice with more info about the meeting. I can make sure you are registered then.

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From: Rubin, Mary (HRSA)
Sent: Monday, March 19, 2018 6:31 AM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: Free trip to Atlanta!

Thanks Narayan. Do I register for the meeting myself or registration is through Muriel?
Mary

From: Nair, Narayan (HRSA)
Sent: Friday, March 16, 2018 2:39 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: Free trip to Atlanta!

Yes, Muriel will be your POC for this travel. She will need some additional info from you.

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E-mail: nnair@hrsa.gov

From: Rubin, Mary (HRSA)
Sent: Friday, March 16, 2018 1:33 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: Free trip to Atlanta!

Yes. I booked the hotel. Should I register? Do I tell Muriel about travel plans? Also regarding hotel

and cab reimbursement – do I give those receipts after I get back?

From: Nair, Narayan (HRSA)
Sent: Friday, March 16, 2018 1:24 PM
To: Rubin, Mary (HRSA) <MRubin@hrsa.gov>
Subject: RE: Free trip to Atlanta!

Just wanted to double check on this are you OK to attend this?

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From: Rubin, Mary (HRSA)
Sent: Monday, March 12, 2018 5:10 PM
To: Nair, Narayan (HRSA) <NNair@hrsa.gov>
Subject: RE: Free trip to Atlanta!

Hi Narayan,

I am interested and likely available.

Mary

From: Nair, Narayan (HRSA)
Sent: Wednesday, March 07, 2018 10:08 AM
To: Dalle-Tezze, Terry (HRSA) <TDalle-Tezze@hrsa.gov>; Ditmar, Mark (HRSA) <MDitmar@hrsa.gov>; Luna, Kenneth (HRSA) <KLuna@hrsa.gov>; Melo, Marco (HRSA) <MMelo@hrsa.gov>; Osborn, Mark (HRSA) <MOsborn@hrsa.gov>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>; Sisk, Nasrin (HRSA) <NSisk@hrsa.gov>; St. Martin, Laura (HRSA) <LStMartin@hrsa.gov>; Stryer, Stacy (HRSA) <SStryer@hrsa.gov>
Subject: Free trip to Atlanta!

I am an ex-officio member of the Advisory Committee of Immunization Practices (ACIP) and may not be able to attend the next meeting that is being held June 20-21 so I was interested in knowing if anyone would be available to attend in my place. Here is some info:

What: The ACIP sets the standard for immunization recommendations. I find the meetings very interesting and learn a lot. Usually they have a vaccine safety update but not always. If you attend you would provide an update to the committee on the VICP activities. It usually is very brief less than 2 minutes. We have a standard script that we use

When: You would fly out Tuesday June 19 and return Thursday evening June 21. The meetings start early Wednesday morning and go a full day. You would be expected to attend in its entirety.

Where: The meeting is at the CDC communications center. This is a very cool building that has the CDC library and a very nice museum that talks about the history of the CDC.

Logistics: Your airfare would be arranged by Muriel. You will not be allowed to pick your own flight.

You would have to pay for hotel/meals/taxi with your credit card but would be reimbursed for these.
I haven't had issues getting reimbursed in a timely manner once I submit my receipts.
Here is a link to the Committee but they haven't posted the agenda for the June meeting yet.
https://www.cdc.gov/vaccines/acip/meetings/meetings-info.html
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From: Nair, Narayan (HRSA)
To: Taylor, Muriel (HRSA)
Cc: Rubin, Mary (HRSA)
Subject: Travel in June
Date: Friday, March 16, 2018 2:40:28 PM

Muriel,

I had a trip scheduled in June but I can't go so Mary is going in my place. This is my June 19-June 21 trip to Atlanta for the ACIP meeting. Can you assist Mary in travel plans?

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From: Nair, Narayan (HRSA)
To: Atanasoff, Sarah (HRSA); Dalle-Tezze, Terry (HRSA); Ditmar, Mark (HRSA); Luna, Kenneth (HRSA); Melo, Marco (HRSA); Osborn, Mark (HRSA); Rubin, Mary (HRSA); Sisk, Nasrin (HRSA); St. Martin, Laura (HRSA); Stryer, Stacy (HRSA)
Cc: Overby, Tamara (HRSA)
Subject: SIRVA on You Tube
Date: Thursday, November 30, 2017 2:37:52 PM

Good afternoon,
As I previously shared the CDC's ACIP spent some time discussing SIRVA at the last meeting in October. They have posted video of the meeting.
https://www.youtube.com/watch?v=jNP88WxtvcU&list=PLvrp9iOILTQb6D9e1YZWpbUvzfptNMKx2&index=3
At the 1 hour 21 minute mark begins the SIRVA discussion and there are presentations by the CDC that discuss outreach/provider education/ and VAERS data.

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Cc:	Overby, Tamara (HRSA)
Subject:	SIRVA materials from CDC
Date:	Tuesday, November 07, 2017 8:35:26 AM
Attachments:	04 Vaccine Safety Kroger.pptx

Good morning,

Here is the presentation that CDC gave at the ACIP outlining their outreach efforts to educate providers about SIRVA.

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Shoulder Injury After Vaccination: CDC/NCIRD Campaign

Andrew Kroger MD, MPH

Medical Officer

Immunization Services Division

Advisory Committee on Immunization Practices

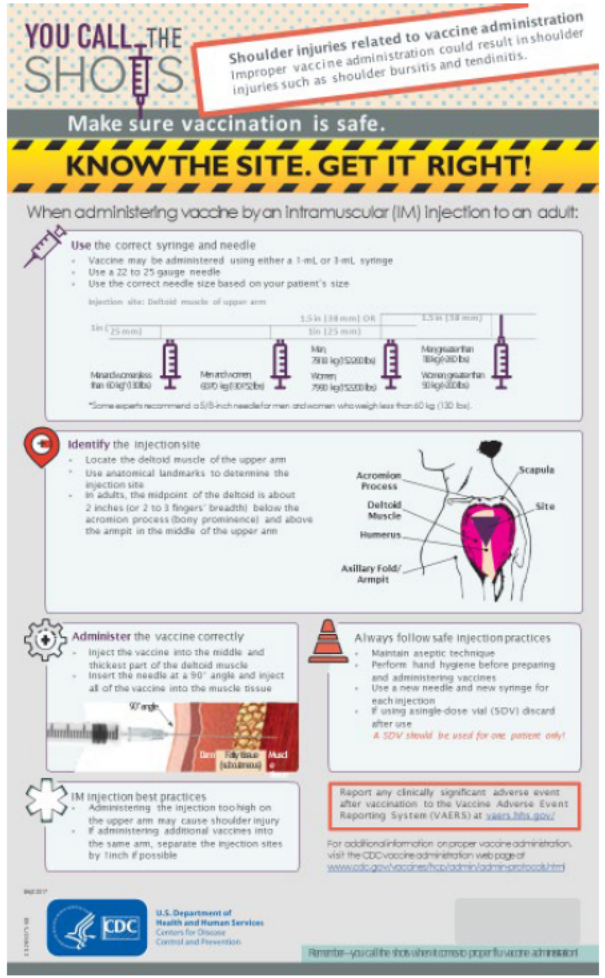
Atlanta, GA

October 25, 2017

Activities

- Phone call with APhA
- Phone call with awardees
- Current Issues in Immunization Netconference Webinar on Influenza
- Release of Infographic and Newsletter Article Template

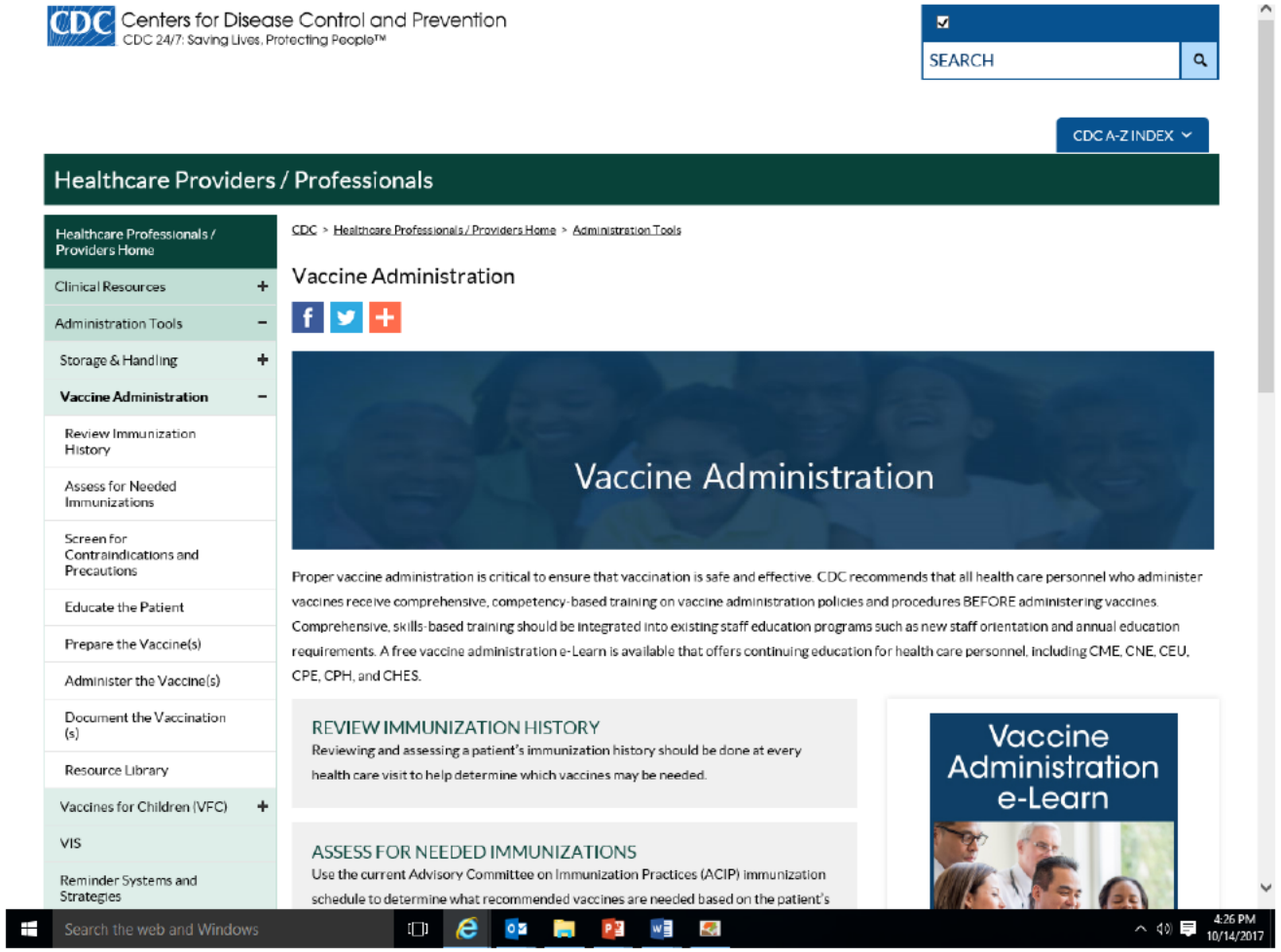
https://www.cdc.gov/vaccines/hcp/infographics/call-the-shots.html



Newsletter Article Template

- Shoulder injuries are preventable with correct IM administration
- Vaccine Administration e-Learn – Posted June 21, 2017
- Vaccine Administration Web page – Posted September 1, 2017
- Shoulder Injuries include bursitis and tendinitis

https://www.cdc.gov/vaccines/hcp/admin/admin-protocols.html



https://www.cdc.gov/vaccines/ed/courses.html.

HRSA000122

Preliminary Campaign Statistics

- A total of 3,411 clicks to CDC web site with 3,108 coming directly from the emails we sent.
  - Remaining 303 clicks were most likely clicks received from other email in which our links were pasted
  - 3,204 clicks came from the United States
- IM video on the YouTube page - 1,235 clicks
- Vaccine Administration resources page - 762 clicks

Acknowledgments

- HRSA
  - Narayan Nair

CDC/NCEZID/DHQP/ISO
  - Frank Destefano
  - Beth Hibbs
  - Tom Shimabukuro

- CDC/NCIRD
  - Dale Babcock
  - Jennifer Hamborsky
  - Lauren Hughes
  - Nancy Messonnier
  - Richard Quartarone
  - Raymond Strikas
  - Falguni Vyas
  - Cindy Weinbaum
  - Joellen Wolicki

From: Nair, Narayan (HRSA)
To: Atanasoff, Sarah (HRSA); Dalle-Tezze, Terry (HRSA); Ditmar, Mark (HRSA); Luna, Kenneth (HRSA); Melo, Marco (HRSA); Osborn, Mark (HRSA); Rubin, Mary (HRSA); Sisk, Nasrin (HRSA); St. Martin, Laura (HRSA); Stryer, Stacy (HRSA)
Subject: SIRVA handouts
Date: Tuesday, October 31, 2017 2:36:47 PM

I have placed some handouts from ACIP related to SIRVA CDC outreach activities from ACIP in the file room for anyone who is interested.

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Cc:	Overby, Tamara (HRSA)
Subject:	SIRVA update at ACIP
Date:	Monday, October 23, 2017 12:53:35 PM
Attachments:	03 Vaccine Safety Shimabukuro.pptx 02 Vaccine Safety Nair.pptx

Good afternoon,

This week I will be attending the Advisory Committee on Immunization Practices (ACIP)in Atlanta. As you know the ACIP includes 15 voting members responsible for making vaccine recommendations for the U.S. adult/pediatric population. This meeting they will be having a 30 minute discussion on SIRVA. I will be presenting our claims data, CDC will be presenting a VAERS study they did on shoulder injuries, and there will be a presentation on CDC's education efforts to avoid vaccination administration errors. I have attached my presentation and the CDC VAERS slides. I don't have their slides discussing their education efforts.

Please don't distribute these slides. Also if you wish to watch the talk the entire meeting is webcast. The SIRVA session will be at 4:30 on Wednesday

Here is the link: https://www.cdc.gov/vaccines/acip/index.html

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Reports of shoulder dysfunction following immunization with inactivated influenza vaccine, Vaccine Adverse Event Reporting System (VAERS), 2010-2016

Tom Shimabukuro, MD, MPH, MBA
Immunization Safety Office
Centers for Disease Control and Prevention (CDC)

Advisory Committee on Immunization Practices
October 25, 2017

Overview

- Background
- Objective
- Methods
- Results (preliminary)
- Summary
- Conclusions

Background: shoulder injury following vaccination

- Atanasoff et al. (2010)[1]
  - Review of 13 claims in the National Childhood Vaccine Injury Program (VICP) between 2006-2010 in which limited and painful range of motion of the shoulder following vaccination was claimed
- Institute of Medicine (2012)[2]
  - Based on Atanasoff et al. paper and other case series and case reports:
    - Evidence convincingly supports a causal relationship between the injection of a vaccine and deltoid bursitis
- Shoulder injury related to vaccine administration (SIRVA) added to the VICP Vaccine Injury Table in 2017[3]

[1]Atanasoff et al. Shoulder injury related to vaccine administration (SIRVA). Vaccine. 2010;28(51):8049-52.
[2] IOM (Institute of Medicine). 2012. Adverse effects of vaccines: Evidence and causality. Washington, DC: The National Academies Press.
[3] National Vaccine Injury Compensation Program: Revisions to the Vaccine Injury Table. A Rule by the Health and Human Services Department. 82 FR 6294. Effective date February 21, 2017. https://www.federalregister.gov/documents/2017/01/19/2017-00701/national-vaccine-injury-compensation-program-revisions-to-the-vaccine-injury-table

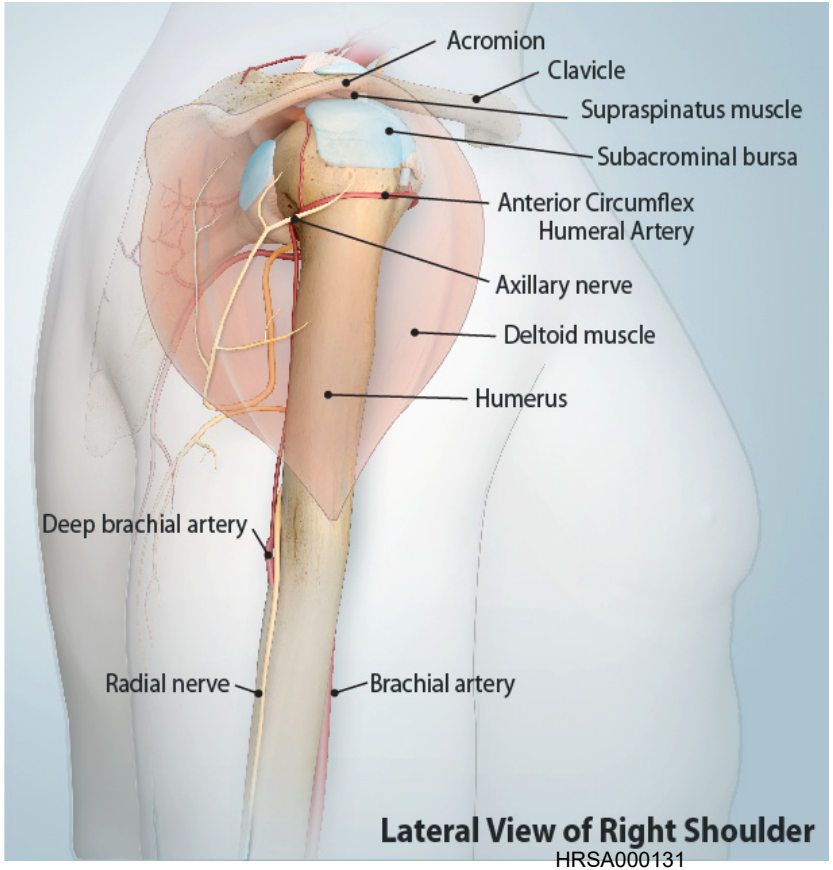
Background: shoulder injury following vaccination[1]

- Shoulder injury related to vaccine administration (SIRVA) manifests as shoulder pain and limited range of motion occurring after the administration of a vaccine intended for intramuscular administration in the upper arm
- These symptoms are thought to occur as a result of unintended injection of vaccine antigen or trauma from the needle into and around the underlying bursa of the shoulder resulting in an inflammatory reaction
- **SIRVA is caused by an injury to the musculoskeletal structures of the shoulder (e.g. tendons, ligaments, bursae, etc.)**
- **SIRVA is not a neurological injury** and abnormalities on neurological examination or nerve conduction studies (NCS) and/or electromyographic (EMG) studies would not support SIRVA as a diagnosis (even if the condition causing the neurological abnormality is not known)

HRSA000130

[1]Reference: Vaccine Injury Table (https://www.hrsa.gov/sites/default/files/vaccinecompensation/vaccineinjurytable.pdf)

Surface landmarks and structures in the upper arm



HRSA000131

Image by Alissa Eckert , CDC Division of Communication Services

Objective

- Describe reports submitted to the Vaccine Adverse Event Reporting System (VAERS) of shoulder dysfunction following immunization (SDFI)[1] with inactivated influenza vaccine (IIV)

[1]VAERS is a passive reporting system and causality generally cannot be assessed using VAERS data alone. Shoulder dysfunction following immunization (SDFI) implies only a temporally associated adverse event of shoulder dysfunction, while shoulder injury related to vaccine administration (SIRVA) implies vaccination caused a shoulder injury.

Vaccine Adverse Event Reporting System (VAERS)[1]

Strengths

- National data
- Accepts reports from anyone
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group
- Generally cannot assess causality
- Coding practices can affect types and numbers of adverse events identified in reports

[1]Vaccine Adverse Event Reporting System: http://vaers.hhs.gov; jointly managed by CDC and FDA

Methods: definition of shoulder dysfunction following immunization with IIV[1]

- Shoulder pain and restricted range of motion following injection of IIV into the upper arm
- Affected shoulder must be of same arm in which IIV was administered alone, with no other concomitant vaccinations
- Exclude reports where more than one vaccination – in addition to IIV – was given in the arm with the affected shoulder (e.g., IIV and PPSV23, Tdap/Td, etc.)
- Onset <48 hours after IIV vaccination
- Symptoms last longer than one week (to differentiate from injection site reactions)
- Exclude reports of neurological injuries (e.g., brachial neuritis)

HRSA000134

[1]Adapted from the Vaccine Injury Compensation Program definition for shoulder injury following vaccine administration (SIRVA) with modification

Methods: VAERS search strategy and case reviews

- Searched VAERS database for reports of shoulder dysfunction following immunization (SDFI) with IIV from July 1, 2010 through June 30, 2016
  - Used MedDRA[1] terms that potentially described shoulder dysfunction and selected vaccine administration error terms
  - And text string search of reports for “arm” or “shoulder”
- All reports identified in initial search were reviewed and classified into three categories: “Not a case,” “Indeterminate case,” or “Possible SDFI case”
- Key information from reports entered into an electronic database using a standardized extraction form in MS Access

[1]Medical Dictionary for Regulatory Activities (https://www.meddra.org/)

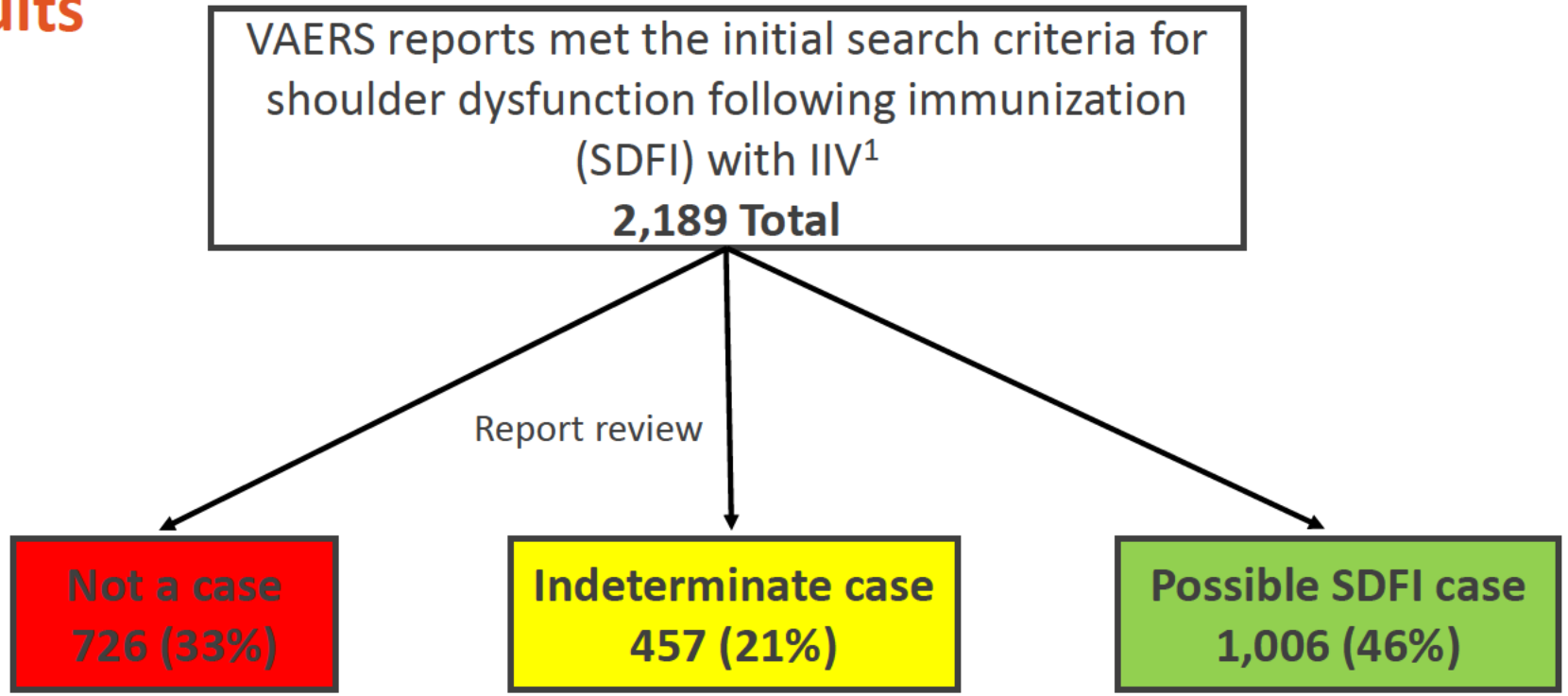
MedDRA Terms used in search for SDFI following IIV

Acute osteomyelitis involving shoulder region
Acute synovitis
Adhesive capsulitis of shoulder
Administration site joint discomfort
Administration site joint effusion
Administration site joint erythema
Administration site joint infection
Administration site joint inflammation
Administration site joint movement impairment
Administration site joint pain
Allergic arthritis involving shoulder region
arthralgia
Arthropathy involving shoulder region
Arthropathy unspecified, involving upper arm
Arthropathy, unspecified, involving shoulder region
Brachialgia
Bursa calcification
Bursa disorder
Bursa injury
Bursal fluid accumulation
Bursal synovitis
Bursitis
Capsulitis of shoulder
Cervicobrachalgia
Cervicobrachial syndrome
drug administration error
Effusion of joint of shoulder region
Effusion of upper arm joint
Injected limb mobility decreased
Injection site joint discomfort
Injection site joint erythema
Injection site joint infection
Injection site joint inflammation
Injection site joint movement impairment
Injection site joint pain
Injury to other specified nerve(s) of shoulder girdle and upper limb
Injury to peripheral nerve(s) of shoulder girdle and upper limb
Joint injury
Joint range of motion decreased
Joint swelling inflammatory
Late effect of injury to peripheral nerve of shoulder girdle and upper limb
Loose body in joint of shoulder region
Neck, shoulder and arm syndrome
Osteoarthrosis, localised, primary, involving shoulder region
Osteoarthrosis, localised, secondary, involving shoulder region
Osteoarthrosis, localized, not specified whether primary or secondary, involving shoulder region
Osteoarthrosis, unspecified whether generalized or localized, involving shoulder region
Other affections of shoulder region, not elsewhere classified
Other and unspecified injury to shoulder and upper arm
Other and unspecified superficial injury of shoulder and upper arm, infected
Other and unspecified superficial injury of shoulder and upper arm, without mention of infection
Other specified arthropathy involving shoulder region
Other specified arthropathy involving upper arm
Other specified crystal arthropathies involving shoulder region
Other specified disorders of bursae and tendons in shoulder region
Other specified disorders of joint of shoulder region
Other symptoms referable to joint of shoulder region
Other symptoms referable to upper arm joint

MedDRA Terms used in search for SDFI following IIV (cont.)

Pain in (l) shoulder
Pain in (r) shoulder
Pain in joint involving shoulder region
Pain in joint involving upper arm
Pain in upper extremities
Palindromic rheumatism involving shoulder region
Periarthritis scapulohumeralis
Purulent synovitis
Pyogenic arthritis involving shoulder region
Rotator cuff syndrome
Rotator cuff syndrome of shoulder and allied disorders
Scapula pain
Shoulder bursitis
Shoulder discomfort
Shoulder dystocia
Shoulder hand syndrome
Shoulder joint pain associated with
Shoulder ligament rupture
Shoulder muscle stiffness
Shoulder osteoarthritis
Shoulder pain
Shoulder pain (due joint disorder)
Shoulder region stiffness of joint, not elsewhere classified, involving upper arm
skeletal injury
Stiffness shoulder
Subacromial bursitis
Synovial cyst
Synovial disorder
Synovial rupture
Synovitis
Synovitis of shoulder
Tendon injury
Tendon rupture
Transient arthropathy involving shoulder region
Transient arthropathy involving upper arm
Traumatic arthritis
Traumatic arthropathy involving shoulder region
Traumatic arthropathy involving upper arm
Traumatic arthrosis
Unspecified disorder of joint of shoulder region
Unspecified disorder of upper arm joint
Unspecified infective arthritis involving shoulder region
Unspecified monoarthritis involving shoulder region
Unspecified monoarthritis involving upper arm
Unspecified osteomyelitis involving shoulder region
Unspecified polyarthropathy or polyarthritis involving shoulder region
Vaccination site joint discomfort
Vaccination site joint effusion
Vaccination site joint erythema
Vaccination site joint infection
Vaccination site joint inflammation
Vaccination site joint movement impairment
Vaccination site joint pain
Vaccination site joint swelling
Villonodular synovitis involving shoulder region
Villonodular synovitis involving upper arm

Results

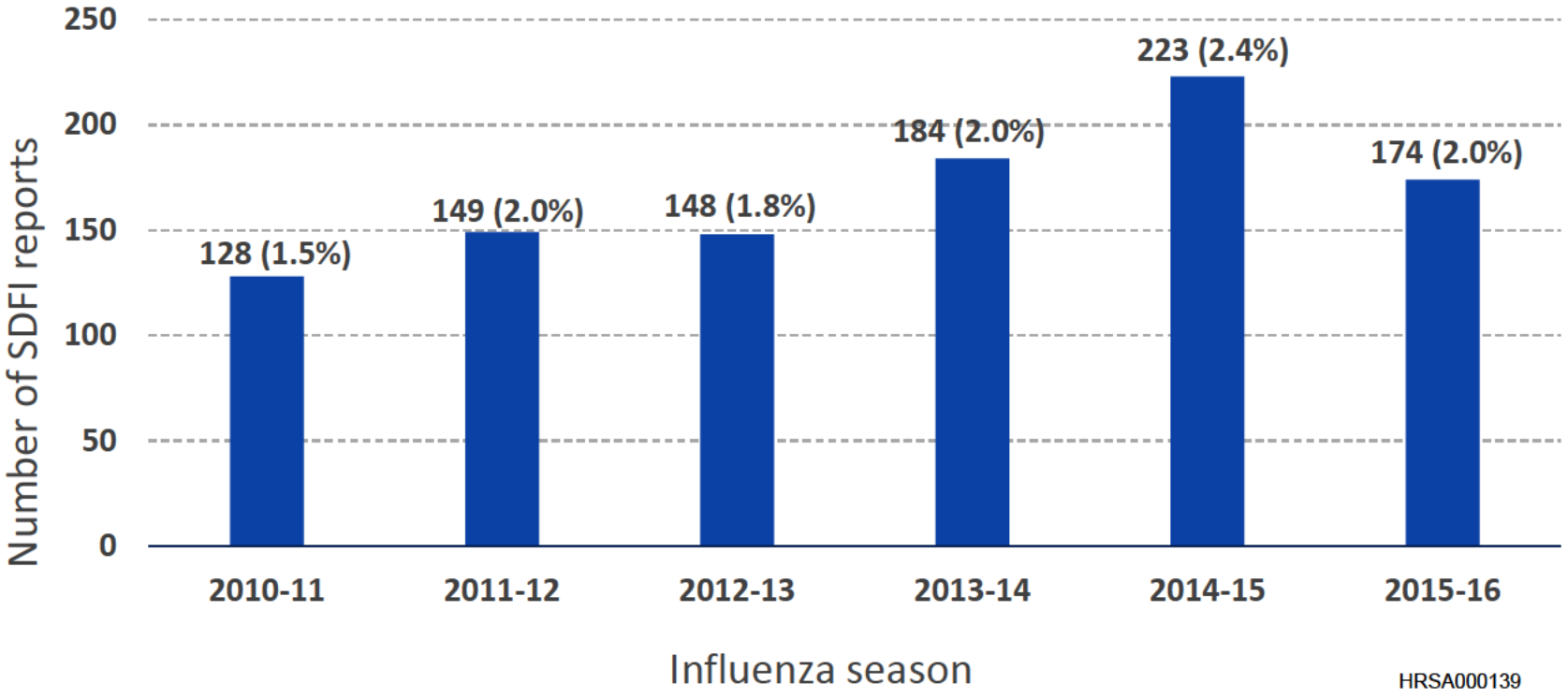


- We included possible SDFI cases following IIV in the preliminary analysis

HRSA000138

[1]VAERS reports vaccinated and received July 1, 2010 through June 30, 2016

VAERS SDFI reports following IIV, N (% among all IIV reports) by influenza season, 2010-2016



Characteristics of VAERS SDFI vs. non-SDFI reports following IIV, July 2010-June 2016

	SDFI following IIV, N (%)	Non-SDFI following IIV, N (%)
Total reports	1,006	50,247
Non-serious	933 (93)	46,707 (93)
Female	829 (82)	34,421 (69)
Median age in years	51 (range 14-94 years)	50 (range 0-102 years)
Age groups		
0-18	6 (<1)	8,541 (17)
19-59	701 (70)	23,709 (47)
60+	288 (29)	16,934 (34)
Unknown	11 (1)	1063 (2)
Type of reporter		
Patient	528 (52)	10,999 (22)
Vaccine provider	273 (27)	23,416 (47)
Manufacturer	36 (4)	4,613 (9)
Other/unknown	169 (17)	11,219 (22)

HRSA000140

Characteristics of VAERS SDFI reports following IIV, July 2010-June 2016

	N (%)
Total reports	**1,006**
Median onset interval[1] (days)	0
Symptoms occurring on day of vaccination	755 (75)
Pain had not resolved at time report was made to VAERS	859 (85)
Seen by healthcare provider for SDFI	496 (49)
Referred to specialist[2]	176 (18)
Orthopedist	130
Surgeon (not specified)	18
Other specialist[3]	47

[1]By definition, onset interval for SDFI is <48 hours following vaccination, day 0 = day of vaccination
[2]Not mutually exclusive
[3]Includes specialist such as rehabilitation medicine, chiropractor, neurologist, acupuncturist, and unspecified "other doctor"

HRSA000141

Characteristics of VAERS SDFI reports following IIV, July 2010-June 2016

Most commonly reported adverse events[1] (N=1,006 total reports)	n (%)
Shoulder pain	442 (44)
Injected limb mobility decreased	407 (41)
Joint range of motion decreased	191 (19)
Drug administered at inappropriate site	156 (16)
Bursitis	94 (9)
Arthralgia	92 (9)
Rotator cuff syndrome	90 (9)
Frozen shoulder	57 (6)
Shoulder bursitis	30 (3)

HRSA000142

[1]MedDRA terms, not mutually exclusive

Reported impact on activities of daily living among VAERS SDFI reports following IIV, July 2010-June 2016

Reported impact on activities of daily living (ADLs) (N=1,006 total reports)	n (%)
Noticeable but does not interfere with ADLs or result in absenteeism from work	4 (1)
Interferes with ADLs, but unknown if it resulted in absenteeism from work	332 (33)
Interferes with ADLs and/or results in absenteeism from work	229 (23)
Unknown/not stated in report how pain affected ADLs and/or absenteeism from work	441 (44)

HRSA000143

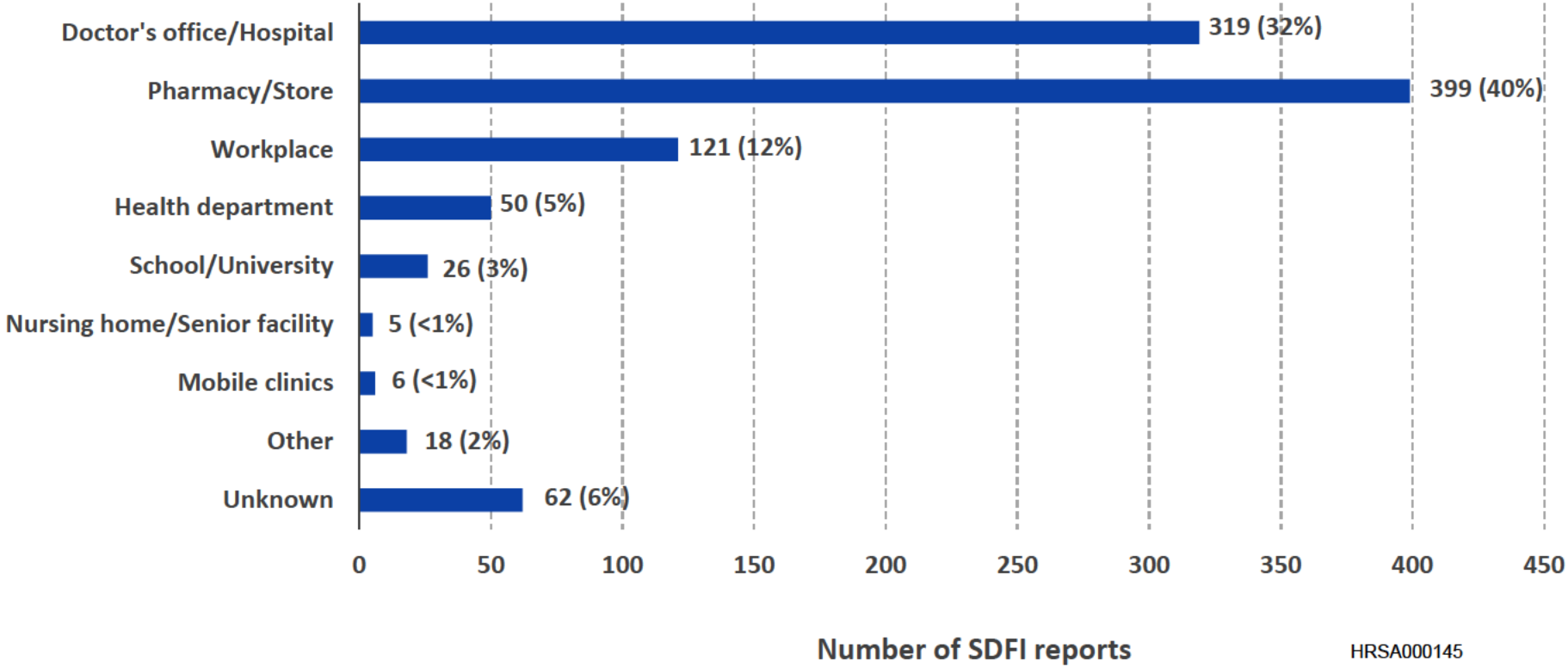
VAERS SDFI reports following IIV where a contributing factor was described (222 of 1,006 reports), July 2010-June 2016

Contributing factors[1] described in narrative (N=222 total reports)	n
Vaccination given too high on arm	177
Improper/poor administration technique	35
Uneven position between vaccinator and patient (vaccinator standing and patient sitting)	5
Other (needle "too long," past history of shoulder pain, etc.)	22

[1]Not mutually exclusive

HRSA000144

Place of vaccination in VAERS SDFI reports following IIV, July 2010-June 2016



HRSA000145

Summary

- Reports to VAERS of SDFI following IIV ranged from 128-223 during the six influenza seasons from 2010-2011 to 2015-2016
  - During that period around 130 million doses of IIV were distributed each influenza season in the United States
- There was a higher percentage of female reports of SDFI following IIV compared to non-SDFI reports
- Most (70%) reports of SDFI following IIV were in the age group 19-59 years; few were in individuals 0-18 years (<1%)
- When possible contributing factors were described, vaccination given too high on the arm was most commonly reported
- The most common place of vaccination documented reports was in pharmacies and doctor's offices/hospitals

Conclusion

- Improperly placed IIV vaccination (or any injectable vaccination) has the potential to cause shoulder injury[1]; however
- Reports to VAERS of SDFI following IIV appear rare, given the amount of IIV distributed in the United States each influenza season
- There does not appear to be a increase in SDFI reports following IIV submitted to VAERS during recent seasons (approximately 2% of all IIV reports during 2010-2011 through 2015-2016 seasons)
- Proper administration technique is important for prevention of SIRVA

Image by Alissa Eckert, CDC Division of Communication Services

HRSA000147

[1] IOM (Institute of Medicine). 2012. Adverse effects of vaccines: Evidence and causality. Washington, DC: The National Academies Press.

Acknowledgements

CDC

Beth Hibbs

Oidda Museru

Pedro Moro

Carmen Ng

Paige Lewis

Maria Cano

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FDA

Jane Woo

Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Update on SIRVA
Advisory Committee on Immunizations Practices

Narayan Nair, MD
Division Director/Chief Medical Officer
Division of Injury Compensation Programs
Healthcare Systems Bureau
Health Resources and Services Administration (HRSA)

SIRVA
Overview

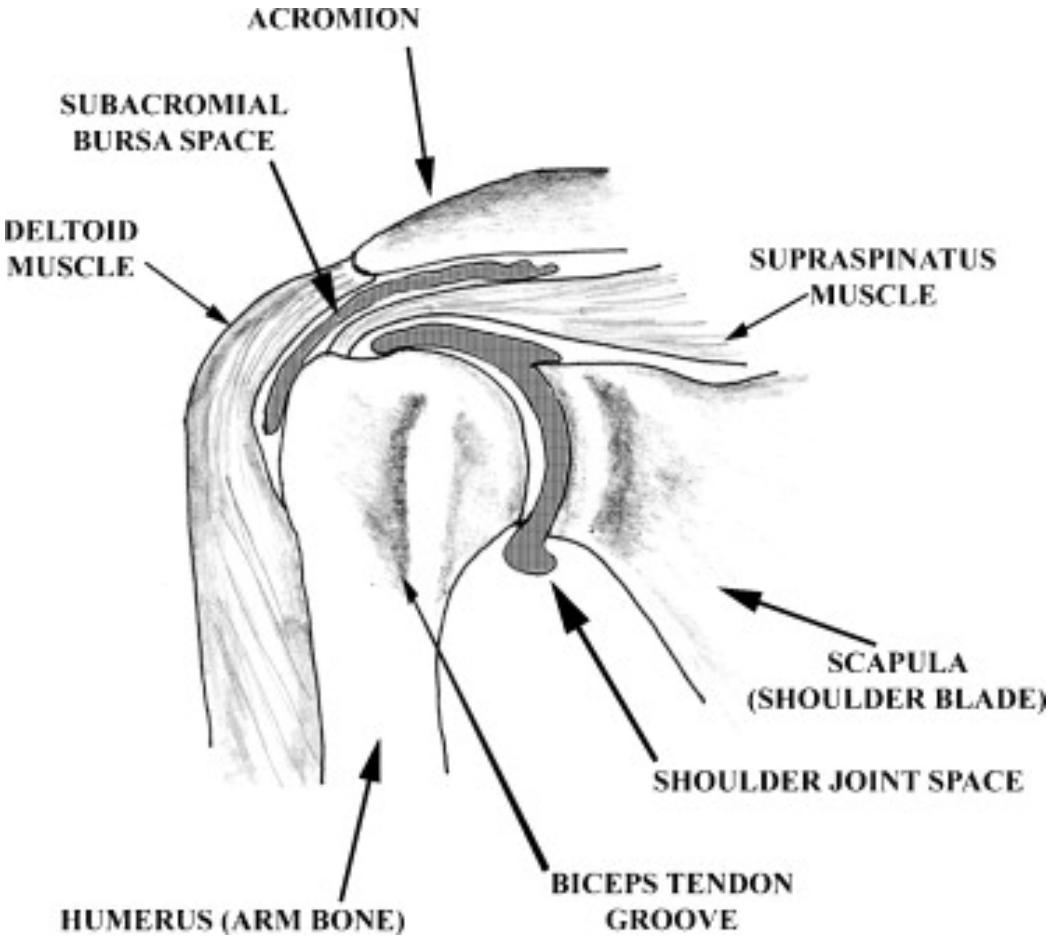
- Background
- DICP Data

SIRVA - Background

- Shoulder Injury Related to Vaccine Administration is thought to result from the unintentional injection of a vaccine into tissues and structures lying underneath the deltoid muscle of the shoulder.
- The Institute of Medicine (IOM) reviewed the scientific and medical literature finding that the evidence convincingly supported a causal relationship between vaccine administration and deltoid bursitis.
- Atanasoff et al. published a case series reporting the experience of the Vaccine Injury Compensation Program with regard to shoulder injuries following vaccination. The IOM reviewed this article and commented that the cases were consistent with deltoid bursitis.

SIRVA

Shoulder anatomy



SIRVA
DICP Data

- Cases/Compensation FY 2011-2016

Fiscal Year	Total Cases	Total Compensation
2011-2014	59	$ 9,699,058
2015	98	$ 12,448,610
2016	202	$ 29,087,666
2017	163	$ 19,921,679

Contact Information

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- nnair@hrsa.gov

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Facebook: facebook.com/HHS.HRSA

From:	Nair, Narayan (HRSA)
To:	Atanasoff, Sarah (HRSA); Buckler, Gretchen (HRSA); Dalle-Tezze, Terry (HRSA); Ditmar, Mark (HRSA); Luna, Kenneth (HRSA); Melo, Marco (HRSA); Osborn, Mark (HRSA); Rubin, Mary (HRSA); Sisk, Nasrin (HRSA); St. Martin, Laura (HRSA); Stryer, Stacy (HRSA)
Cc:	Overby, Tamara (HRSA)
Subject:	ACIP update
Date:	Sunday, June 25, 2017 10:03:08 PM

Good evening,

Last week I attended the Advisory Committee on Immunization Practices (ACIP) in Atlanta. Below is a brief summary:

ACIP June 2017 Recap – Day One

- Dr. Arthur Reingold (ACIP), a departing member of ACIP, introduced the Hepatitis A section, noting that the recommendations have not been updated since 2006. He announced that the working group will present a statement with updated recommendations for vote in Oct. 2017 or Feb. 2018.
    - Working group proposes updating language by adding recommendation for catch up vaccine (children 2-18), encouraging vaccine during pregnancy, and aligning language for chronic liver disease patients with recommendations for Hepatitis B.
- Alicia Budd of the CDC provided an update on influenza surveillance, reporting that 130,000 cases were reported during the 2016-17 season – 70% of cases were Flu A.
- Several presenters noted that GSK's Shingrix vaccine, which is under development, could potentially be more cost effective than Zostavax due to its minimal waning and higher rate of vaccine effectiveness.
- Dr. Rafael Harpaz presented on the effectiveness of the varicella vaccination program, noting that varicella cases have steeply declined in all age groups since the introduction of the vaccine in 1996. He denied the correlation between the introduction of the varicella vaccine and the growth of herpes zoster cases by explaining how cases began increasing prior to 1996 and noting that there is no evidence to prove a causal link.
- In an update on Hepatitis B vaccine supply, Dr. Jean Santoli announced that Merck will not distribute the vaccine through the end of 2017, but GSK has the supply to fill this gap in stock.

ACIP June 2017 Recap – Day Two

- Dr. Mona Marin of the CDC provided an update on mumps surveillance, reporting that nearly 3,300 mumps cases have been reported in 2017. She discussed a number of contributing factors for recent outbreaks, including vaccine effectiveness, waning immunity, force of infection, antigenic strains vs. vaccine strains, and other several other factors.
- Dr. Cristina Cardemil of the CDC presented on the effectiveness of MMR3 during a mumps outbreak at a highly-vaccinated university, concluding that MMR3 was associated with a decreased incidence of mumps. However, outbreak control is the composite of several factors, including health department coordination and MMR2 uptake.
- Dr. Tom Shimabukuro reported that VAERS will rollout VAERS 2.0, a new reporting form with revised data elements and updated processes for submitting VAERS reports. From June 30, 2017 to December 2017, VAERS and CDC will implement the VAERS 2.0 form and phase out the VAERS-1 form.

Narayan Nair, MD
CAPT, USPHS
Division Director/Chief Medical Officer

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Health Resources and Services Administration
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From: Nair, Narayan (HRSA)
To: Herzog, Andrea (HRSA); Calvo, Ahmed (HRSA); Johnson, Amber (HRSA); Balingit-Wines, Ana (HRSA); Herzog, Andrea (HRSA); Atanasoff, Sarah (HRSA); Beach, Scott (HRSA); Lee, Cheryl A. (HRSA); Marks, Carole (HRSA); Mishler, Dale (HRSA); Dalle-Tezze, Terry (HRSA); Ditmar, Mark (HRSA); Buckler, Gretchen (HRSA); Jackson, Jean (HRSA); Soodak, Joel H. (HRSA); St. Martin, Laura (HRSA); St. Martin, Laura (HRSA); Luna, Kenneth (HRSA); Melo, Marco (HRSA); Rubin, Mary (HRSA); Taylor, Muriel (HRSA); Sisk, Nasrin (HRSA); Osborn, Mark (HRSA); Saunders, Richard (HRSA); Stryer, Stacy (HRSA); Overby, Tamara (HRSA); Esposito, Vincent (HRSA); Sorensen, Ward (HRSA)
Subject: Status this week
Date: Monday, February 20, 2017 9:04:52 PM

Good evening,
I will be speaking at the FDA tomorrow. I will then be departing for CDC in Atlanta to attend the ACIP. I return Thursday evening. Although I will have my out of office on, I will periodically check email. Have a great week.

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From: Buckler, Gretchen (HRSA)
To: Atanasoff, Sarah (HRSA); Sisk, Nasrin (HRSA); Luna, Kenneth (HRSA); Nair, Narayan (HRSA); Dalle-Tezze, Terry (HRSA); Ditmar, Mark (HRSA); Melo, Marco (HRSA); Osborn, Mark (HRSA); Rubin, Mary (HRSA); St. Martin, Laura (HRSA); Stryer, Stacy (HRSA)
Subject: RE: Anti-vaccine statements from Cleveland Clinic physician
Date: Sunday, January 08, 2017 11 05:05 PM

I saw this on social media yesterday and was also able to open the link in Narayan's email. I also came across this apology from this article reporting the apology from the author of the blog as well as Cleveland Clinic's promise to discipline him - http://www.cleveland.com/healthfit/index.ssf/2017/01/cleveland_clinic_doc_apologizes_for_anti_vax_column_hospital_promises_discipline.html
The apology wasn't very good - "I apologize and regret publishing a blog that has caused so much concern and confusion for the public and medical community. I fully support vaccinations and my concern was meant to be positive around the safety of them."
Hope everyone had a good weekend,
Gretchen

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CDR, USPHS
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Rockville, MD 20857
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Fax: 301-443-8196
abuckler@hrsa.gov

From: Atanasoff, Sarah (HRSA)
Sent: Sunday, January 08, 2017 4:56 PM
To: Sisk, Nasrin (HRSA) <NSisk@hrsa gov>; Luna, Kenneth (HRSA) <KLuna@hrsa.gov>; Nair, Narayan (HRSA) <NNair@hrsa.gov>; Buckler, Gretchen (HRSA) <ABuckler@hrsa.gov>; Dalle-Tezze, Terry (HRSA) <TDalle-Tezze@hrsa.gov>; Ditmar, Mark (HRSA) <MDitmar@hrsa gov>; Melo, Marco (HRSA) <MMelo@hrsa.gov>; Osborn, Mark (HRSA) <MOsborn@hrsa.gov>; Rubin, Mary (HRSA) <MRubin@hrsa gov>; St. Martin, Laura (HRSA) <LStMartin@hrsa.gov>; Stryer, Stacy (HRSA) <SStryer@hrsa gov>
Subject: RE: Anti-vaccine statements from Cleveland Clinic physician
I got "page not found" maybe they pulled it.

From: Sisk, Nasrin (HRSA)
Sent: Sunday, January 08, 2017 4:29 PM
To: Luna, Kenneth (HRSA) <KLuna@hrsa.gov>; Nair, Narayan (HRSA) <NNair@hrsa.gov>; Atanasoff, Sarah (HRSA) <SAtanasoff@hrsa.gov>; Buckler, Gretchen (HRSA) <ABuckler@hrsa.gov>; Dalle-Tezze, Terry (HRSA) <TDalle-Tezze@hrsa.gov>; Ditmar, Mark (HRSA) <MDitmar@hrsa gov>; Melo, Marco (HRSA) <MMelo@hrsa.gov>; Osborn, Mark (HRSA) <MOsborn@hrsa.gov>; Rubin, Mary (HRSA) <MRubin@hrsa gov>; St. Martin, Laura (HRSA) <LStMartin@hrsa.gov>; Stryer, Stacy (HRSA) <SStryer@hrsa gov>
Subject: RE: Anti-vaccine statements from Cleveland Clinic physician
I couldn't…..

From: Luna, Kenneth (HRSA)
Sent: Sunday, January 08, 2017 3:45 PM
To: Nair, Narayan (HRSA) <NNair@hrsa gov>; Atanasoff, Sarah (HRSA) <SAtanasoff@hrsa.gov>; Buckler, Gretchen (HRSA) <ABuckler@hrsa.gov>; Dalle-Tezze, Terry (HRSA) <TDalle-Tezze@hrsa.gov>; Ditmar, Mark (HRSA) <MDitmar@hrsa gov>; Melo, Marco (HRSA) <MMelo@hrsa.gov>; Osborn, Mark (HRSA) <MOsborn@hrsa.gov>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>; Sisk, Nasrin (HRSA) <NSisk@hrsa.gov>; St. Martin, Laura (HRSA) <LStMartin@hrsa gov>; Stryer, Stacy (HRSA) <SStryer@hrsa.gov>
Subject: RE: Anti-vaccine statements from Cleveland Clinic physician
CAPT et al,
I was unable to open the first link. Did anyone else open it?
V/r
Ken

From: Nair, Narayan (HRSA)
Sent: Sunday, January 08, 2017 10:42 AM
To: Atanasoff, Sarah (HRSA) <SAtanasoff@hrsa.gov>; Buckler, Gretchen (HRSA) <ABuckler@hrsa.gov>; Dalle-Tezze, Terry (HRSA) <TDalle-Tezze@hrsa.gov>; Ditmar, Mark (HRSA) <MDitmar@hrsa.gov>; Luna, Kenneth (HRSA) <KLuna@hrsa gov>; Melo, Marco (HRSA) <MMelo@hrsa.gov>; Osborn, Mark (HRSA) <MOsborn@hrsa.gov>; Rubin, Mary (HRSA) <MRubin@hrsa.gov>; Sisk, Nasrin (HRSA) <NSisk@hrsa.gov>; St. Martin, Laura (HRSA) <LStMartin@hrsa gov>; Stryer, Stacy (HRSA) <SStryer@hrsa.gov>
Subject: Anti-vaccine statements from Cleveland Clinic physician
Good morning,
A couple of links I wanted to share some anti-vaccine sentiments from a physician that are somewhat notable in that the person is medical director and chief operating officer of the Cleveland Clinic Wellness Institute:
http://www.cleveland.com/lyndhurst-south-euclid/index.ssf/2017/01/make_2017_the_year_to_avoid_to.html#incart_email
In addition here is a rebuttal from the science writer at Forbes Magazine:
http://www forbes com/sites/tarahaelle/2017/01/07/cleveland-clinic-goes-full-anti-vaccine/#11755cb0408c

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