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**From:** Bailey, Steven R.  
**Sent:** Thu, 13 Aug 2015 21:21:04 +0000  
**To:** Winiecki, Scott (FDA/CBER);Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Bailey, Steven R.  
**Subject:** FW: CIOMS WG Updated distribution list for TG2 manual  
**Attachments:** Vaccine\_Safety\_WG\_Combined\_Business\_Plan\_2015mar30~Novi.pptx, Ch1-VM7--150319 -- SRB -- 20150414 (IC) (3) srb update-cgm-kh.docx, Table of passive active tools\_2mar srb.docx, Ch2-VM6-150112 BRAZILIAN REV\_SKW\_20150127.docx, Ch3-VM7-150319 fxd 150615~Novi.docx, 5.2 Who should set up.docx, CIOMS-TG2-GACVS-maure-2014dec22.docx, Draft Communication-sn.docx, Ethical concepts for ActSS\_gsf\_hvd.docx, CIOMS Vaccine Safety WG TG 1\_outline\_kh\_20150722\_MB\_kh.doc, TG3 Draft chapter up to 2 4 for commenting\_29 July 2015 pz\_kh.docx

Frank/Scott:

As we get ready for our next meeting here in Philadelphia (I certainly hope you are joining us), Karin is beginning to organize where each group stands. I will work with her to ready WG2 (apparently I am now the lead), and will meet with her on Tuesday.

Ahead of my talking with her, could you just update me where we are with Chapters 2 and 3? Karin has attached what she believes is the latest version, but I would assume you might have already addressed the comments you have received, and might have a more updated version than what has been passing through the e-mail ether.

More importantly, could you give me your perspective of what the next steps are (from you perspective) for your chapters, and how we can best use the 2 days together to move them to completion? That way I can build an agenda that can productively give you all the feedback/additional materials/etc. to finish our work.

Thanks in advance your consideration, and if you could send an update before I meet with Karin on Tuesday morning it would be appreciated.

Regards,

Steven

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmkarin@cioms.ch]  
**Sent:** Thursday, August 13, 2015 5:43 AM  
**To:** Bailey, Steven R.  
**Subject:** FW: CIOMS WG Updated distribution list for TG2 manual

Dear Steven,

Thanks for everything you have been doing to ensure a good meeting in September!

I am trying to find out where we stand on TG2 the manual and wonder if you could give me an overview on where we stand and where I can help over the next week or so to get things ready for the Philly meeting? We need to think of how to structure the agenda to be most productive. We have no outside speakers planned, except you are welcome to invite a senior Pfizer person to open, if you wish. We must obviously focus on making most use of our face-to-face to progress on deliverables.

Attached please find the latest versions as I understand for the various sections of the entire WG:\*

1. WG Combined Business Plan (incl. Chart of Chapters)
2. TG1 Essential Vaccine Information Document
3. TG2 Manual on Active Safety Surveillance
  - a. Chapter 1
  - b. Chapter 2
  - c. Chapter 3
  - d. Other Sections Drafts
4. TG3 Vaccine Safety Communication

\*Please note that the person responsible may not as yet have incorporated all comments received from WG members in the version attached.

After I hear from you on any updates for TG2, I will send the same complete group of files to the heads of topic group 1 (Uli Heininger) and topic group 3 (Priya Bahri). If you would like to discuss by phone, let me know a good date/time for you?

Kind regards,  
Karin

**Karin R. Holm**

Technical Collaboration Coordinator, CIOMS WG on Vaccine Safety  
CIOMS IX Risk Minimisation and CIOMS X Meta-Analysis  
Council for International Organizations of Medical Sciences (CIOMS)  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)

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**From:** Holm Karin [<mailto:holm@cioms.ch>]

**Sent:** Tuesday, August 04, 2015 4:39 PM

**To:** Novilia; Bailey ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com)); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mimi ([mimidar@hva.gov](mailto:mimidar@hva.gov)); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Holm Karin; Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kurz, Xavier

([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Martin ([David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Nishioka, Sergio ((b)(6)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sillan, Françoise ([Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com)); Sjolín\_Forsberg Gunilla; Tebaa, Amina ((b)(6)); Ulf Bergman ([ulf.bergman@karolinska.se](mailto:ulf.bergman@karolinska.se)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int)); Heiles, Bernhard ([bernhard.heiles@merck.com](mailto:bernhard.heiles@merck.com))

**Cc:** Le\_Roux Susanne

**Subject:** CIOMS WG Updated distribution list for TG2 manual

My updated distribution list for CIOMS WG on Vaccine Safety, topic group 2 on the manual for active safety surveillance.

**Adding to distribution:** Rebecca Chandler (new UMC), Bernard Heiles (new merck), Karin Holm (I didn't have myself on it!), Sue le Roux (CIOMS new administrative person)

**Removing due to leaving WG:** Fabio Leviano, Sten Olsson

**Karin R. Holm**

Publications Consultant, WG IX Risk Minimisation

Technical Coordinator, WG on Vaccine Safety

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland

Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)

Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

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**From:** Bailey, Steven R.  
**Sent:** Fri, 15 Jul 2016 12:49:40 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID); Holm Karin; Zuber, Patrick (CDC who.int); 'Bachtiar, Novilia (novilia@biofarma.co.id)'; 'Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com)'; 'Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu)'; 'Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br)'  
**Cc:** Rago Lembit  
**Subject:** RE: Post-TC version Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July

Frank:

Thanks. I think this is a real improvement over our old text. A question for you and the group: (b)(4)

(b)(4)

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Wednesday, July 13, 2016 5:05 PM  
**To:** Bailey, Steven R.; Holm Karin; Zuber, Patrick (CDC who.int); 'Bachtiar, Novilia (novilia@biofarma.co.id)'; 'Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com)'; 'Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu)'; 'Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br)'  
**Cc:** Rago Lembit  
**Subject:** RE: Post-TC version Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July

In the comment boxes I have proposed revised text (b)(4)

(b)(4)

Frank

Frank DeStefano, MD, MPH

---

**From:** Bailey, Steven R. [mailto:Steven.R.Bailey@pfizer.com]  
**Sent:** Tuesday, July 12, 2016 4:19 PM

**To:** Holm Karin <[holm@cioms.ch](mailto:holm@cioms.ch)>; Zuber, Patrick (CDC who.int) <[zuberp@who.int](mailto:zuberp@who.int)>; 'Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id))' <[novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)>; 'Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com))' <[Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)>; 'Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu))' <[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)>; 'Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br))' <[Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)>; Destefano, Frank (CDC/OID/NCEZID) <[fxd1@cdc.gov](mailto:fxd1@cdc.gov)>

**Cc:** Rago Lembit <[ragol@cioms.ch](mailto:ragol@cioms.ch)>

**Subject:** RE: Post-TC version Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July

Karin/All:

In the attached, please find my 3 items of home work: I have updated the 3 sections suggested. Happy to take feedback now, or after incorporated into the larger document.

I have also reached out to Scott, and will be speaking with him in the next few days if we can find the time.

And whenever you are ready to review the updated EVI-whatever table, reach out and we will set up some time to review together, and then with Uli.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Holm Karin [<mailto:holm@cioms.ch>]

**Sent:** Tuesday, July 12, 2016 10:41 AM

**To:** Bailey, Steven R.; 'Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))'; 'Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id))'; 'Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com))'; 'Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu))'; 'Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br))'; 'DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov))'

**Cc:** Rago Lembit

**Subject:** Post-TC version Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July

Dear Ed Bd,

Thank you for your efforts and active TC. Almost there! Attached is new version with assignments "master 12 July\_TC". Send your comments to Steven and me however is easiest for you.

Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety  
Publications Coordinator, CIOMS X Meta-Analysis  
Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland  
Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)  
(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)

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**From:** Holm Karin

**Sent:** 12 July 2016 13:50

**To:** Bailey, Steven ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int)); Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov))

**Cc:** Rago Lembit

**Subject:** Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July

Dear Ed Board,

Attached please find the latest version. We have included recent comments from Patrick, Corinne, and Novi (and okay from Frank). I have not yet to incorporate Irina's recent edits. But we can discuss at TC.

Best, Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety  
Publications Coordinator, CIOMS X Meta-Analysis  
Council for International Organizations of Medical Sciences (CIOMS)  
c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland  
Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)  
(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)



**From:** Kuter, Barbara J.  
**Sent:** Wed, 15 May 2013 14:01:37 -0400  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: intussusception presentation

Frank,

Thanks for this information. Yes, we have seen the Shui paper from 2012, but it only covered the data until 2010. Are you saying the results of the updated analysis are fairly similar to the Shui 2012 publication?

I will check to see if there are any questions on the VAERS data. Thanks for allowing us the opportunity to ask questions on both.

Barb

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Wednesday, May 15, 2013 1:42 PM  
**To:** Kuter, Barbara J.  
**Subject:** RE: intussusception presentation

Barbara,

We will be presenting the VAERS data at ACIP plus an update on the VSD analysis. It is the updated VSD analysis that we would like to preview for you on May 31. If you would also like us to address questions about the VAERS data, we can do that as well. I was not planning on sending slides out beforehand. The findings are fairly straight-forward, especially if you are familiar with the Shui 2012 publication.

Thanks,  
Frank

---

**From:** Kuter, Barbara J. [mailto:barbara\_kuter@merck.com]  
**Sent:** Monday, May 13, 2013 7:26 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: intussusception presentation

Hi Frank,

I just saw the VAERS data published in *Pediatrics* today – congratulations! Are these the data you will be presenting at ACIP or is there another update?

The VSD data were last published by Shui et al in 2012. That analysis was based on data through Feb 2010. I assume you have now analyzed additional data, perhaps through 2012?

If possible, it would be helpful if we could receive a copy of the slides you will be presenting prior to the May 31 teleconference. That way, we can review the data & be prepared with questions. Please let me know if that would be possible.

Thanks.

Barb

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Wednesday, May 08, 2013 11:02 AM  
**To:** Kuter, Barbara J.  
**Subject:** RE: intussusception presentation

Let's go with 10:30-11:30. Call details to follow.

---

**From:** Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
**Sent:** Wednesday, May 08, 2013 10:16 AM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: intussusception presentation

Frank,

I checked calendars again and it looks like Friday, May 31 would be good for us. How about either 10:30-11:30, 3-4, or 4-5?

Thanks.

Barb

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Tuesday, May 07, 2013 1:25 PM  
**To:** Kuter, Barbara J.  
**Subject:** RE: intussusception presentation

Barb,

Next week will not work for us. We were thinking of doing the presentation in the last week of May or the first week of June. Do you have availability during those weeks? Thanks for the offer to arrange a Webex; I'll let you know, but I think we can take care of that on our end.

Thanks,

Frank

---

**From:** Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
**Sent:** Monday, May 06, 2013 5:28 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: intussusception presentation

Frank,

I've checked calendars & May 13 from 1-2 pm or May 14 from 11-12 would be best. Would either work for your team? And will you be sharing slides? If so, we could arrange for some sort of Webex.

Thanks.

Barb

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Monday, May 06, 2013 9:33 AM  
**To:** Kuter, Barbara J.  
**Subject:** RE: intussusception presentation

Yes, an hour should be adequate.

---

**From:** Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
**Sent:** Monday, May 06, 2013 8:11 AM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: intussusception presentation

I will get a few dates from this end. Will an hour suffice, please?

Thanks.

Barb

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Friday, May 03, 2013 3:14 PM  
**To:** Kuter, Barbara J.  
**Subject:** RE: intussusception presentation

We could set up the teleconference if you could provide some times that would work for you over the next few weeks.

Thanks,  
Frank

---

**From:** Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
**Sent:** Friday, May 03, 2013 12:59 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** Re: intussusception presentation

Frank,

Thanks for your note. Yes, we would greatly appreciate a preview of the data. How do you want to arrange that?



Barb

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Friday, May 03, 2013 12:36 PM  
**To:** Kuter, Barbara J.  
**Subject:** intussusception presentation

Hi Barbara,

I think you know that at the June ACIP meeting there will be a session on rotavirus vaccines and intussusception. As part of that session we will be presenting updated data from VAERS and VSD on RotaTeq and intussusception. If you are interested, we would be willing to arrange a teleconference to provide you and a limited number of Merck staff members a confidential preview of the presentations.

Best regards,  
Frank

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA

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**From:** Bailey, Steven R.  
**Sent:** Tue, 12 Jul 2016 20:19:19 +0000  
**To:** Holm Karin; Zuber, Patrick (CDC who.int); 'Bachtiar, Novilia (novilia@biofarma.co.id)'; 'Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com)'; 'Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu)'; 'Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br)'; Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Rago Lembit  
**Subject:** RE: Post-TC version Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July  
**Attachments:** Cioms guide AVSS\_master\_12 July\_TC srb.docx

Karin/All:

In the attached, please find my 3 items of home work: I have updated the 3 sections suggested. Happy to take feedback now, or after incorporated into the larger document.

I have also reached out to Scott, and will be speaking with him in the next few days if we can find the time.

And whenever you are ready to review the updated EVI-whatever table, reach out and we will set up some time to review together, and then with Uli.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** Tuesday, July 12, 2016 10:41 AM  
**To:** Bailey, Steven R.; 'Zuber, Patrick (zuberp@who.int)'; 'Bachtiar, Novilia (novilia@biofarma.co.id)'; 'Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com)'; 'Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu)'; 'Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br)'; 'DeStefano, Frank (fxd1@cdc.gov)'  
**Cc:** Rago Lembit  
**Subject:** Post-TC version Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July

Dear Ed Bd,

Thank you for your efforts and active TC. Almost there! Attached is new version with assignments "master 12 July\_TC". Send your comments to Steven and me however is easiest for you.

Karin

**Karin R. Holm**  
Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis  
Council for International Organizations of Medical Sciences (CIOMS)  
c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland  
Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)  
(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)

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**From:** Holm Karin  
**Sent:** 12 July 2016 13:50  
**To:** Bailey, Steven ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int)); Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov))  
**Cc:** Rago Lembit  
**Subject:** Vaccine Safety Guide AVSS - Ed Bd TC Tues 12 July

Dear Ed Board,

Attached please find the latest version. We have included recent comments from Patrick, Corinne, and Novi (and okay from Frank). I have not yet to incorporate Irina's recent edits. But we can discuss at TC.

Best, Karin

**Karin R. Holm**  
Technical Collaboration Coordinator, Working Group on Vaccine Safety  
Publications Coordinator, CIOMS X Meta-Analysis  
Council for International Organizations of Medical Sciences (CIOMS)  
c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland  
Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)  
(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)

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**From:** Bailey, Steven R.  
**Sent:** Wed, 25 May 2016 16:27:10 +0000  
**To:** Straus, Walter L.; Holm Karin; Abdoellah, Siti (alt) (b)(6); Arlett, Peter (Peter.Arlett@ema.europa.eu); Ayoub, Ayman; Bachtiar, Novilia (novilia@biofarma.co.id); Bahri, Priya (Priya.Bahri@ema.europa.eu); Benkirane, Raja (b)(6) Bergman, Ulf (b)(6) Blum, Michael (michael.blum222@comcast.net); Bonhoeffer, Jan (alt) (j.bonhoeffer@brightoncollaboration.org); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Ceuppens, Marc (mceuppe1@its.jnj.com); Chandler, Rebecca (alt) (rebecca.chandler@who-umc.org); Darko, Mimi (b)(6); Dawei, Liu (liudw929@126.com); Destefano, Frank (CDC/OID/NCEZID); Dadoo, Alex (b)(6) n); 'Dong Duo (dongduo@cdr-adr.org.cn)'; Gregory, William (NYC); Gunale, Bhagwat (alt) (bhagwat.gunale@seruminstitute.com); 'HAMID (regobpom@indo.net.id)'; Heiles, Bernhard; Heining, Ulrich (ulrich.heining@ukbb.ch); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); Keller-Stanislawski (Brigitte.Keller-Stanislawski@pei.de); Kilpi, Terhi (terhi.kilpi@thl.fi); Kulkarni, Prasad (drpsk@seruminstitute.com); Kurz, Xavier (Xavier.Kurz@ema.europa.eu); Lindquist, Marie (Marie.Lindquist@who-umc.org); Maroko, Robert; Maure, Christine (maurec@who.int); Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br); Mentzer, Dirk (Dirk.Mentzer@pei.de); Nishioka, Sergio (b)(6); Nohynek Anna (Hanna.Nohynek@thl.fi); Oberle, Doris (alt2) (Doris.Oberle@pei.de); Patel, Mayur (alt) (PatelMayur@MedImmune.com); Ramkishan, Ajmeer (b)(6); 'Rauscher, Martina (martina.rauscher@takeda.com)'; Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Seifert, Harry (Harry.A.Seifert@gsk.com); Shimabukuro, Tom (CDC/OID/NCEZID); Srivastava, Swati (alt) (b)(6); Tebaa, Amina (b)(6); 'Wang, Yali (alt2) (wangyali@cdr-adr.org.cn)'; Winiecki, Scott (FDA/CBER); Youssef, Mona (b)(6); Zuber, Patrick (CDC who.int)  
**Cc:** Rago Lembit  
**Subject:** RE: CIOMS issue of information sharing on vaccine safety between private and public stakeholders  
**Importance:** High

Dear All:

So far, we have only received the response from Walter below regarding how to handle information sharing in our guide.

Given the timing (we are just about 1 month from going to print, we are going to move forward with the proposed solution. We still welcome further comments, and esp. suggested text that anyone is willing to provide.

In order to finalize this last piece, we are going to schedule a meeting to discuss and finalize the text for this issue. For simplicity, we will use a weekly Editorial Board meeting that was already schedule for Friday, June 3<sup>rd</sup>, at 9:00 AM EDT. I will shortly invite all of you to this meeting, and anyone who is interested in contributing is welcome to join. We would esp. appreciate participation by anyone who has raised this concern, and those who have provided feedback (such as Walter).

If you are particularly interested in this topic, but cannot attend, let me know and we will see if we can move the meeting.

Please note that we will move forward after that meeting with the consensus opinion reached then.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Straus, Walter L. [mailto:walter\_straus@merck.com]  
**Sent:** Sunday, May 22, 2016 7:28 PM  
**To:** Bailey, Steven R.; Holm Karin; Abdoellah, Siti (alt) (b)(6) Arlett, Peter (Peter.Arlett@ema.europa.eu); Ayoub, Ayman; Bachtiaf, Novilla (novilla@biorama.co.id); Bahri, Priya (Priya.Bahri@ema.europa.eu); Benkirane, Raja (raja.benkirane@gmail.com); Bergman, Ulf (b)(6) Blum, Michael (michael.blum222@comcast.net); Bonhoeffer, Jan (alt) (j.bonhoeffer@brightoncollaboration.org); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Ceuppens, Marc (mceuppe1@its.jnj.com); Chandler, Rebecca (alt) (rebecca.chandler@who-umc.org); Darko, Mimi (r (b)(6)); Dawei, Liu (liudw929@126.com); DeStefano, Frank (fxd1@cdc.gov); Dodoo, Alex ( (b)(6) Dong Duo (dongduo@cdr-adr.org.cn); Gregory, William (NYC); Gunale, Bhagwat (alt) (bhagwat.gunale@seruminstitute.com); 'HAMID (regobpom@indo.net.id); Heiles, Bernhard; Heininger, Ulrich (ulrich.heininger@ukbb.ch); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofi-pasteur.com); Keller-Stanislawski (Brigitte.Keller-Stanislawski@pei.de); Kilpi, Terhi (terhi.kilpi@thl.fi); Kulkarni, Prasad (drpsk@seruminstitute.com); Kurz, Xavier (Xavier.Kurz@ema.europa.eu); Lindquist, Marie (Marie.Lindquist@who-umc.org); Maroko, Robert; Maure, Christine (maurec@who.int); Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br); Mentzer, Dirk (Dirk.Mentzer@pei.de); Nishioka, Sergio ( (b)(6) ); Nohynek Anna (Hanna.Nohynek@thl.fi); Oberle, Doris (alt2) (Doris.Oberle@pei.de); Patel, Mayur (alt) (PatelMayur@MedImmune.com); Ramkishan, Ajmeer ( (b)(6) 'Rauscher, Martina (martina.rauscher@takeda.com); Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Seifert, Harry (Harry.A.Seifert@gsk.com); Shimabukuro, Tom (alt) (ayv6@cdc.gov9); Srivastava, Swati (alt) (b)(6); Tebaa, Amina (atebaa@yahoo.fr); 'Wang, Yali (alt2) (wangyali@cdr-adr.org.cn); Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov); Youssef, Mona (b)(6) Zuber, Patrick (zuberp@who.int)  
**Cc:** Rago Lembit  
**Subject:** RE: CIOMS issue of information sharing on vaccine safety between private and public stakeholders

Dear WG:

Thanks to Karin for summarizing these outstanding issues.

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Best,

*Walter*

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**Walter L. Straus, MD, MPH, FCPP, FACP** Associate Vice President and Therapeutic Area Head, Clinical Safety and Risk Management 2 (Infectious Diseases and Vaccines), Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 /Fax: 215-616-1095

Assistant: Jane Detweiler [jane\\_detweiler@merck.com](mailto:jane_detweiler@merck.com) Tel: 267-305-7027

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]

**Sent:** Sunday, May 22, 2016 4:41 PM

**To:** Holm Karin; Abdoellah, Siti (alt) ([asfyabd@hotmail.com](mailto:asfyabd@hotmail.com)); Arlett, Peter



([Peter.Arlett@ema.europa.eu](mailto:Peter.Arlett@ema.europa.eu)); Ayoub, Ayman; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Benkirane, Raja ((b)(6)); Bergman, Ulf ((b)(6)); Blum, Michael ((b)(6)); Bonhoeffer, Jan (alt) ([j.bonhoeffer@brightoncollaboration.org](mailto:j.bonhoeffer@brightoncollaboration.org)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Ceuppens, Marc ([mceuppe1@its.jnj.com](mailto:mceuppe1@its.jnj.com)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mimi ((b)(6)); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ((b)(6)); 'Dong Duo' ([dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn)); Gregory, William (NYC); Gunale, Bhagwat (alt) ([bhagwat.gunale@seruminstitute.com](mailto:bhagwat.gunale@seruminstitute.com)); 'HAMID' ([regobbpom@indo.net.id](mailto:regobbpom@indo.net.id)); Heiles, Bernhard; Heininger, Ulrich ([ulrich.heininger@ukbb.ch](mailto:ulrich.heininger@ukbb.ch)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Keller-Stanislawski ([Brigitte.Keller-Stanislawski@pei.de](mailto:Brigitte.Keller-Stanislawski@pei.de)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kulkarni, Prasad ([drpsk@seruminstitute.com](mailto:drpsk@seruminstitute.com)); Kurz, Xavier ([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Lindquist, Marie ([Marie.Lindquist@who-umc.org](mailto:Marie.Lindquist@who-umc.org)); Maroko, Robert; Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Mentzer, Dirk ([Dirk.Mentzer@pei.de](mailto:Dirk.Mentzer@pei.de)); Nishioka, Sergio ((b)(6)); Nohynek Anna ([Hanna.Nohynek@thl.fi](mailto:Hanna.Nohynek@thl.fi)); Oberle, Doris (alt2) ([Doris.Oberle@pei.de](mailto:Doris.Oberle@pei.de)); Patel, Mayur (alt) ([PatelMayur@MedImmune.com](mailto:PatelMayur@MedImmune.com)); Ramkishan, Ajmeer ((b)(6)); 'Rauscher, Martina' ([martina.rauscher@takeda.com](mailto:martina.rauscher@takeda.com)); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Shimabukuro, Tom (alt) ([ayv6@cdc.gov9](mailto:ayv6@cdc.gov9)); Srivastava, Swati (alt) ((b)(6)); Straus, Walter L.; Tebaa, Amin ((b)(6)); 'Wang, Yali' (alt2) ([wangyali@cdr-adr.org.cn](mailto:wangyali@cdr-adr.org.cn)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Youssef, Mona ((b)(6)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Rago Lembit; Bailey, Steven R.

**Subject:** RE: CIOMS issue of information sharing on vaccine safety between private and public stakeholders

All:

I wanted to follow up on Karin's e-mail, as we have not received any response back to date. As we near the end of our process, and will be finalizing the document in the next month, it is critical that we resolve this issue in a timely manner. To make it very clear, this is what we are looking for:

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- b. We will request participation in a working session to complete this additional language. Currently, we have scheduled Editorial Board sessions on Fridays from 9 to 11, US east coast time. We would propose either May 27<sup>th</sup> or June 3<sup>rd</sup>, during these times to get together a group of interested parties. So, if you wish (or can) to contribute to this important effort, and want your voice to be heard, please let us know your availability for these times on either or both of the 27<sup>th</sup> and 3<sup>rd</sup>. And if you cannot make either of these times, but feel strongly about participating, let us know some other times, and we will see if we can arrange a telecon at another time.

Again, our time is quickly coming to a close, and addressing this piece with thoughts from the entire group is critical. If you have an opinion, please express it, and, more importantly, please propose some text and/or participate in a working session to help us complete this piece of our document.

Kind regards,

Steven (on behalf of the Editorial Board)

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Holm Karin [<mailto:holmkarin@cioms.ch>]

**Sent:** Friday, May 13, 2016 12:03 PM

**To:** Abdoellah, Siti (alt) (b)(6); Arlett, Peter ([Peter.Arlett@ema.europa.eu](mailto:Peter.Arlett@ema.europa.eu)); Ayoub, Ayman; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Bailey, Steven R.; Benkirane, Raja (b)(6); Bergman, Ulf (b)(6); Blum, Michael (b)(6); Bonhoeffer, Jan (alt) ([j.bonhoeffer@brightoncollaboration.org](mailto:j.bonhoeffer@brightoncollaboration.org)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Ceuppens, Marc ([mceuppe1@its.jnj.com](mailto:mceuppe1@its.jnj.com)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mimi (b)(6); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex (b)(6); 'Dong Duo' ([dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn)); Gregory, William (NYC); Gunale, Bhagwat (alt) ([bhagwat.gunale@seruminstitute.com](mailto:bhagwat.gunale@seruminstitute.com)); 'HAMID' ([regobpom@indo.net.id](mailto:regobpom@indo.net.id)); 'Heiles, Bernhard'; Heininger, Ulrich ([ulrich.heininger@ukbb.ch](mailto:ulrich.heininger@ukbb.ch)); Holm Karin; Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Keller-Stanislawski ([Brigitte.Keller-Stanislawski@pei.de](mailto:Brigitte.Keller-Stanislawski@pei.de)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kulkarni, Prasad ([drpsk@seruminstitute.com](mailto:drpsk@seruminstitute.com)); Kurz, Xavier ([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Lindquist, Marie ([Marie.Lindquist@who-umc.org](mailto:Marie.Lindquist@who-umc.org)); Maroko, Robert; Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Mentzer, Dirk ([Dirk.Mentzer@pei.de](mailto:Dirk.Mentzer@pei.de)); Nishioka, Sergio (b)(6); Nohynek Anna ([Hanna.Nohynek@thl.fi](mailto:Hanna.Nohynek@thl.fi)); Oberle, Doris (alt2) ([Doris.Oberle@pei.de](mailto:Doris.Oberle@pei.de)); Patel, Mayur (alt) ([PatelMayur@MedImmune.com](mailto:PatelMayur@MedImmune.com)); Ramkishan, Ajmeer (dr (b)(6)); 'Rauscher, Martina' ([martina.rauscher@takeda.com](mailto:martina.rauscher@takeda.com)); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Shimabukuro, Tom (alt) ([ayv6@cdc.gov](mailto:ayv6@cdc.gov)); Srivastava, Swati (alt) (s (b)(6)); 'Straus, Walter' ([walter\\_straus@merck.com](mailto:walter_straus@merck.com)); Tebaa, Amina (b)(6); Tang, Yali (alt2)



([wangyali@cdr-adr.org.cn](mailto:wangyali@cdr-adr.org.cn)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Youssef, Mona ([reg\\_affairs@who.int](mailto:reg_affairs@who.int)) (b)(6) Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Rago Lembit

**Subject:** CIOMS issue of information sharing on vaccine safety between private and public stakeholders

Dear CIOMS WG on Vaccine Safety,

Some industry members of the WG have recently expressed their concern that the WG has not been able to solve the issue of h (b)(4)

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The original scope and concept note for the CIOMS Working Group on Vaccine Safety centered around collaboration on guidance documents on harmonized tools and methods for the conduct of vaccine pharmacovigilance. This WG was conceived to address the WHO's Global Vaccine Safety Initiative (GVSII) aims to promote a more efficient and rapid collection and exchange of information about vaccine safety issues between national regulatory authorities, vaccine manufacturers and multilateral agencies. The working group was proposed to serve as well as a "think-tank" that would develop and propose new approaches in the field.

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We wanted to respond to this concern broadly and ask the entire working group what they think to get a sense where everyone stands. While we cannot adequately address this in the current WG, we are looking to you to provide your thoughts and suggestions, so that some additional language can be crafted with an eye towards suggesting future action. To go beyond our current deliverable plan would probably require more brainstorming and a focused approach with regulators. That could be one of the purposes for a future WG.

That being said we would like to get a wider sense of how the group feels about this topic, and look to you to participate in whatever we draft. The Editorial Board is making an explicit call for suggestions and perhaps a few volunteers to collate and craft the response into a working draft, and this is your chance to be part of the dialogue. We need the entire working group to stand behind whatever suggestions are raised if it will become as part of recommendations in the final document.

This working group could and maybe *should* recommend strategies in the report to remedy this, suggest areas needing further attention, and point out ways

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This is

an important issue and we look for your active engagement to address it by volunteering to join an *ad hoc* group to actually write the text **before Wednesday 1 June** so we can circulate for consideration by the WG and for discussion by the Editorial Board TC meeting on Friday 3 June.

Thank you for your efforts and expertise.

Kind regards,  
Karin Holm

**Karin R. Holm**

Technical Coordinator, Working Group on Vaccine Safety  
Publications Consultant, Working Group IX Risk Minimization  
Council for International Organizations of Medical Sciences (CIOMS)  
Associate partner of UNESCO / In official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

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your system.

**From:** Straus, Walter L.  
**Sent:** Sun, 31 Jan 2016 14:10:01 -0500  
**To:** MAURE, Christine; Bailey, Steven R.; Caplanusi Irina; Destefano, Frank (CDC/OID/NCEZID); Wivel, Ashley E.; Corinne.Jouquelet-Royer@sanofipasteur.com; Winiecki, Scott (FDA/CBER); holmk@cioms.ch; novilia@biofarma.co.id; ulf (b)(6) com; (b)(6) o.co.uk; dongduo@cdr.gov.cn; Rmenezes@bio.fiocruz.br; sergio.de.andrade.nishioka@gmail.com; Paulo.santos@bio.fiocruz.br; Harry.A.Seifert@gsk.com; sjolinforsbergg@cioms.ch; atebaa@yahoo.fr; Zuber, Patrick (CDC who.int); Maroko, Robert; 董铎  
**Cc:** Rantz, Reggie  
**Subject:** RE: CIOMS TG1 Final Draft Review - COMMENTS PROVIDED  
**Attachments:** CIOMS TG1 Intro and Chapters 1-3-ws.docx

Dear All,

Thanks for sharing the document for review

I've added numerous suggestions to strengthen the document.

Many of the comments focus upon several issues:

(b)(4)

Best regards,

*Walter*

---

**Walter L. Straus, MD, MPH, FCPP, FACP** Associate Vice President and Therapeutic Area Head, Clinical Safety and Risk Management 2 (Infectious Diseases and Vaccines), Merck Research Laboratories, Merck & Co., Inc., 351 North Summeytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 / Fax: 215-616-1095  
Assistant: Jane Detweiler jane\_detweiler@merck.com Tel: 267-305-7027

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**From:** MAURE, Christine [mailto:maurec@who.int]  
**Sent:** Friday, January 29, 2016 9:06 AM  
**To:** Bailey, Steven R.; Caplanusi Irina; Destefano, Frank (CDC/OID/NCEZID); Wivel, Ashley E.; Corinne.Jouquelet-Royer@sanofipasteur.com; Winiecki, Scott (FDA/CBER); holmk@cioms.ch;



novilia@biofarma.co.id; (b)(6) mimidarko66@yahoo.co.uk;  
dongduo@cdr.gov.cn; Rmenezes@bio.fiocruz.br; sergio.de.andrade.nishioka@gmail.com;  
Paulo.santos@bio.fiocruz.br; Harry.A.Seifert@gsk.com; sjolinforsbergg@cioms.ch;  
atebaa@yahoo.fr; ZUBER, Patrick Louis F.; Maroko, Robert; 董铎

**Cc:** Rantz, Reggie; Straus, Walter L.

**Subject:** RE: CIOMS TG1 Final Draft Review

Many thanks Steven for putting this together.

Please find attached some comments on this revised version for consideration. Happy to discuss further during the upcoming call.

Best regards  
Christine

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]

**Sent:** 14 January 2016 16:54

**To:** Caplanusi Irina; Destefano, Frank (CDC/OID/NCEZID); MAURE, Christine; Wivel, Ashley E.;  
[Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); Winiecki, Scott (FDA/CBER); [holm@cioms.ch](mailto:holm@cioms.ch);  
[novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6) (b)(6)

[dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); [sergio.de.andrade.nishioka@gmail.com](mailto:sergio.de.andrade.nishioka@gmail.com);  
[Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforsbergg@cioms.ch](mailto:sjolinforsbergg@cioms.ch); [atebaa@yahoo.fr](mailto:atebaa@yahoo.fr);  
ZUBER, Patrick Louis F.; Maroko, Robert; 董铎

**Cc:** Rantz, Reggie; Straus, Walter L.

**Subject:** CIOMS TG1 Final Draft Review

All:

In preparation for our telecon and webex scheduled for February 4<sup>th</sup>, I am attaching a consolidated version of all our work to date. The attached document contains the overall document introduction, and then Chapters 1, 2 and 3. The prime authors of each chapter have consolidated and responded to all comments received to date. Any comments remaining are those that still need to be addressed by this group at our meeting (e.g., comments where there is not alignment across all the group).

A few other notes:

- 1) There is quite a bit of new text that has not been seen by the larger group yet:
  - a. The introduction will be new to those that did not work on it
  - b. Table 3.4 and accompanying text which was updated by Novi and Irina (numbering changed since they updated)
  - c. Section 3.5 which was updated by Scott (numbering changed since he wrote it)
  - d. Section 3.7, the ethical aspects, updated by Christine.

I have highlighted all of these new section in GREEN TEXT and you may wish to pay extra attention to these section and consider sending comments on them TO THE AUTHOR of that section and copy the group. We will have to come up a with a process for update this new master document appropriately.

- 2) There appears to have been some loss of version control along the way, and there is now some overlap and difference in text between sections 3.4 and 3.5. Could I request Frank (probably with Scott) take a look at these two sections, and determine how they should be best consolidated. I am not sure what happened, and perhaps I simply confused the various versions that had been sent to me for consolidation.

I will be travelling extensively between now and the 4<sup>th</sup>, so it is unlikely I will be able to do further work on this document. This should be the version we will use for our discussion. At that meeting we can discuss any additional changes and comments that you may have and how these can be incorporated. Also, given I will not be able to attend the meeting in Ghana, we will need to discuss who will take over the next drafts of this master document.

Kind regards,

Steven.

Chapter Authors: (Scott, Frank and I) please be prepared to walk through all open questions on your sections, and raise any issues/questions you need in order to have sections finalized before Ghana.

Many thanks,  
Steven.

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~~~~~

**\*Steven to host\***

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Access code: 642 (b)(6)

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**From:** Bailey, Steven R.  
**Sent:** Fri, 23 Oct 2015 20:21:42 +0000  
**To:** Holm Karin;Bachtiar, Novilia (novilia@biofarma.co.id);Bergman, Ulf  
(b)(6);Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu);Darko, Mimi  
(b)(6);Destefano, Frank (CDC/OID/NCEZID);Duo, Dong  
(dongduo@cdr.gov.cn);Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com);Maure,  
Christine (maurec@who.int);Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br);Nishioka, Sergio  
(b)(6);Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br);Seifert, Harry  
(Harry.A.Seifert@gsk.com);Sjolin\_Forsberg Gunilla;Tebaa, Amina (b)(6);Winiecki, Scott  
(FDA/CBER);Zuber, Patrick (CDC who.int)  
**Cc:** Ashley Wivel (ashley.wivel@merck.com);Maroko, Robert;dongduo@cdr-  
adr.org.cn  
**Subject:** RE: Some Meeting Follow Up  
**Attachments:** CIOMS Manual on Vaccine Active Safety Surveillance - 06092015 (3) srb.docx  
**Importance:** High

All:

We are just 1 week away from our first set of deadlines for TG2 (November 1<sup>st</sup> if a week from this Sunday), and I want to make sure we were moving along, and either encourage everyone to provide updates, or, if necessary, rework our deliverable date.

From our business plan, here is what is due by November 1<sup>st</sup>:

- Thorough review of Chapters 1, 2 and 3, with track changes/comments to Chapter owners **(ALL)**
- Chapter 3: Table 3.3, Section 3.4: Update/Write: **(Novi/Irina)**
- Chapter 3: Sections 3.5 and 3.6: Update/Write: **(Scott)**
- Introduction: Update/Write section 1 (intro), section 2 (algorithm), section 3 (RACI): **(Steven)**
- Introduction: Write Section 4 (structure approach to reviewing data) **(Ashley/Rob (draft 1))**
- Ethical Section (end of chapter 3 now): Carefull Review/update: **(ALL)**

Per previous e-mail, I have already completed bullet 4 and circulated. I am now providing my thorough review of the first 3 chapters, with special attention to the ethical section (see attached).

Hoping this encourages everyone to move forward with the above. However, I do understand how busy schedules are, so let's see how everyone does over the coming week, and we can consider moving our deadlines as needed. Also, based on where we are, I would like to set up a telecon of the group in mid November or so to go over any open items or issues.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory

SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Bailey, Steven R.

**Sent:** Monday, October 12, 2015 12:58 PM

**To:** Holm Karin; Bachtiar, Novilia (novilia@biofarma.co.id); Bergman, Ulf (b)(6); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Darko, Mimi (b)(6); DeStefano, Frank (fxd1@cdc.gov); Duo, Dong (dongduo@cdr.gov.cn); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); Maure, Christine (maurec@who.int); Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br); Nishioka, Sergio (b)(6); Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Seifert, Harry (Harry.A.Seifert@gsk.com); Sjolín\_Forsberg Gunilla; Tebaa, Amina (b)(6); Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov); Zuber, Patrick (zuberp@who.int)

**Cc:** Ashley Wivel (ashley.wivel@merck.com); Maroko, Robert; 'dongduo@cdr-adr.org.cn'

**Subject:** RE: Some Meeting Follow Up

**Importance:** High

All:

Hope everyone is well. I wanted to make sure we were still keeping up the momentum for TG2. So I have gone ahead and completed one of my deliverables for the project. Please find attached a DRAFT of an update to the Introduction. It includes 3 of the 4 pieces: the opening, the RACI, and the Algorithm.

The last piece of the intro is the (b)(4)

(b)(4) Ashley and Rob have agreed to take a stab at adding this piece (first draft), and my hope is that by providing this it will be helpful in moving this forward. Ashley/Rob: please reach out if needed as we move this forward.

Please keep in mind the remaining activities per our business plan:

For November 1<sup>st</sup>:

- All to review Chapters 1, 2, and 3 very carefully. Please send your comments to all, and the owner of each section will consolidate those comments and provide the next draft. Please note the revised drafts are due November 23<sup>rd</sup>, so it is very important that you provide your comments by NOVEMBER 1<sup>st</sup>, as discussed. [as a reminder, Chapter Owners are Chapter 1: Steven, Chapter 2: Scott, Chapter 3: Frank]
- Novi/Irina/Scott: Chapter 3 has some sections that still need to be completed, and you all kindly "volunteered" to work on these sections (Table 3.3/section 3.4 (Irina/Novi) and section 3.5/3.6 (Scott))
- All: Review the "ethical section" of chapter 3, with an eye towards how it fits with the rest of the chapter, and any required changes.

I know we committed to tight timelines, but it would be great if we can deliver. If we can work on the 3 bullets above by the 1<sup>st</sup> of November, we really will be in good shape to have all of our deliverables finalized (per our group) before the year-end holidays, and allow review by the larger group before we all meet in Ghana.



If anyone feels a telecon would be helpful at any point in the process (this entire group, or a subset), please let me know and we will work to arrange.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Bailey, Steven R.

**Sent:** Wednesday, September 30, 2015 4:48 PM

**To:** Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bergman, Ulf (b)(6); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi (b)(6); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Nishioka, Sergid (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sjolín\_Forsberg Gunilla; Tebaa, Amina (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert; Bailey, Steven R.

**Subject:** Some Meeting Follow Up

All (Primarily TG 2 members and key stakeholders)

Please find attached some promised documents (sorry for the delay).

Attached are:

- 1) The Updated Business Plan for TG2. Please pay special attention to your assignments and due dates in the business plan. I will send reminders in about 2 weeks to try to keep us on track. Please feel free to offer updates or suggestions if I missed anything.
- 2) Attached is our preliminary RACI. Will require more work as we move forward, but a good start.
- 3) The latest draft of the Introduction that we discussed at the meeting. Ashley, Rob, Scott and others who offered to work on this (including myself), please compare against the business plan for what we agreed to as next steps. If anyone feels a small telecon to further discuss the intro is needed, do not hesitate to request, and I can arrange.

It was a pleasure seeing most of you in Collegeville, and for those who could not attend, look forward to seeing you in Ghana. I will trust everyone will move forward with our work as outlined in the business plan, and will check in in a few weeks. If any questions, please reach out.

Regards,

Steven

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Holm Karin [<mailto:holmkarin@cioms.ch>]

**Sent:** Thursday, September 24, 2015 11:03 AM

**To:** Abdoellah, Siti (alt) (b)(6); Arlett, Peter ([Peter.Arlett@ema.europa.eu](mailto:Peter.Arlett@ema.europa.eu)); Ayoub, Ayman; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Bailey, Steven R.; Benkirane, Raja (b)(6); Bergman, Ulf (b)(6); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)); Bonhoeffer, Jan (alt) ([j.bonhoeffer@brightoncollaboration.org](mailto:j.bonhoeffer@brightoncollaboration.org)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Ceuppens, Marc ([mceuppe1@its.inj.com](mailto:mceuppe1@its.inj.com)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mim (b)(6); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ([alex.dodoo@umcafrica.org](mailto:alex.dodoo@umcafrica.org)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Gregory, William (NYC); Gunale, Bhagwat (alt) ([bhagwat.gunale@seruminstitute.com](mailto:bhagwat.gunale@seruminstitute.com)); HAMID, T. Bahdar Johan (b)(6); Heiles, Bernhard <[bernhard.heiles@merck.com](mailto:bernhard.heiles@merck.com)>; Heininger, Ulrich ([ulrich.heininger@ukbb.ch](mailto:ulrich.heininger@ukbb.ch)); Holm Karin; Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Keller-Stanislawski ([Brigitte.Keller-Stanislawski@pei.de](mailto:Brigitte.Keller-Stanislawski@pei.de)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kulkarni, Prasad ([drpsk@seruminstitute.com](mailto:drpsk@seruminstitute.com)); Kurz, Xavier ([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Lindquist, Marie ([Marie.Lindquist@who-umc.org](mailto:Marie.Lindquist@who-umc.org)); Martin, David ([David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Mentzer, Dirk ([Dirk.Mentzer@pei.de](mailto:Dirk.Mentzer@pei.de)); Nishioka, Sergio (b)(6); Nohynek Anna ([Hanna.Nohynek@thl.fi](mailto:Hanna.Nohynek@thl.fi)); Oberle, Doris (alt2) ([Doris.Oberle@pei.de](mailto:Doris.Oberle@pei.de)); Patel, Mayur (alt) ([PatelMayur@MedImmune.com](mailto:PatelMayur@MedImmune.com)); Ramkishan, Ajmeer (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Shimabukuro, Tom (alt) ([ayv6@cdc.gov9](mailto:ayv6@cdc.gov9)); Sjolín, Forsberg Gunilla; Srivastava, Swati (alt) (b)(6); Tebaa, Amina (alt) (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Youssef, Mona ([reg\\_affairs@who.int](mailto:reg_affairs@who.int)) (b)(6); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Le\_Roux Susanne; Habersaat, Katrine (DCE-VPI); Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert

**Subject:** Philly meeting group photo

Dear All,

Sending you the group photo from the Philadelphia meeting, which I think reflects on our faces the positive feelings we had about what we achieved at this meeting.

I will also shortly be sending you information about how to access the SharePoint website in an easier manner to get the latest drafts and background documents (I have not yet posted all the updates but shall in coming few weeks).

You will also receive within the coming few weeks, the Philly meeting report so that everyone will feel up-to-date and ready to contribute to this next phase of further writing and editing. Even if you have had little time to involve yourself until now, the Editorial Team can really use your help, expertise, and support to produce a useful guide to Vaccine Safety for new and new-to-you (as we were calling them for short) vaccines.



Please be already planning on attending the next 8<sup>th</sup> meeting to be hosted in Accra, Ghana by the Ghana Food and Drugs Authority, in March or April 2016, as announced by Mimi Darko on the second day of our meeting. We will be sending out a doodle to help determine the best date.

Best regards,  
Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holm@cioms.ch](mailto:holm@cioms.ch)

*(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)*

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**From:** Angus.Thomson@sanofipasteur.com  
**Sent:** Mon, 21 Sep 2015 09:32:12 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** OFFIT@email.chop.edu  
**Subject:** FW: Chapter on Vaccine Hesitancy for Vaccines 7th Edition

Dear Dr. Destefano,

I am contacting you on the advice of Paul Offit, following Stanley Plotkin's suggestion to include a section on vaccine hesitancy in the Vaccine Safety chapter of the 7<sup>th</sup> Ed of Vaccines.

Our thinking on vaccine hesitancy has moved a long way since the 6<sup>th</sup> Ed, in particular in our understanding of the limited effects of information and education on people's attitudes, and more broadly in our understanding of the social and behavioural drivers of vaccination behavior.

Thus, it is important that I frame the 1500 words I have drafted well within the context of the draft chapter you have. Paul suggested I ask you for the most recent draft so that I can do my best to tailor a section (and save you both any trouble with the integration of this section).

Could you please send me what you have?

Your sincerely,

Angus Thomson  
Angus Thomson PhD  
Senior Director, Vaccination Policy & Advocacy - Sanofi Pasteur  
2 Ave Pont Pasteur, 69367 Lyon Cedex 7, France  
@ThomsonAngus | tel: + 33 4 37 66 96 86 | cell: + 33 6 71 29 98 50  
What vaccination advocacy should look like: [https://www.youtube.com/watch?v=DDOh4\\_qzhM](https://www.youtube.com/watch?v=DDOh4_qzhM)

---

**From:** Offit, Paul [mailto:OFFIT@email.chop.edu]  
**Sent:** Saturday, September 19, 2015 12:38 PM  
**To:** Thomson, Angus (sanofi pasteur)  
**Subject:** RE: Chapter on Vaccine Hesitancy for Vaccines

Angus,

Please contact Frank DeStefano at the CDC to get the latest version of our Safety chapter. It would be better to try to integrate your section into the most recent version.

Thanks,

Paul

---

**From:** [Angus.Thomson@sanofipasteur.com](mailto:Angus.Thomson@sanofipasteur.com) <[Angus.Thomson@sanofipasteur.com](mailto:Angus.Thomson@sanofipasteur.com)>  
**Sent:** Friday, September 18, 2015 10:38 AM  
**To:** [stanley.plotkin@vaxconsult.com](mailto:stanley.plotkin@vaxconsult.com); [Stanley.Plotkin@sanofipasteur.com](mailto:Stanley.Plotkin@sanofipasteur.com)  
**Cc:** Offit, Paul  
**Subject:** RE: Chapter on Vaccine Hesitancy for Vaccines

OK, I will aim to have it to Paul early next week.

Paul, I hope this is not throwing a spanner in your works - I realise you have already drafted something, and don't want to give you more work. I am currently working from the previous chapter (6<sup>th</sup> Ed) to try to integrate some of the sections you wrote with what I have. If you were able to send me the latest version of the chapter, I could do this as best as possible so that you have a head start when looking at how to integrate it.

Best regards,

Angus

---

**From:** Stanley Plotkin [<mailto:stanley.plotkin@vaxconsult.com>]  
**Sent:** Thursday, September 17, 2015 2:48 PM  
**To:** Thomson, Angus (sanofi pasteur); Plotkin, Stanley (sanofi pasteur/EXT)  
**Cc:** Watson, Michael (sanofi pasteur); [OFFIT@email.chop.edu](mailto:OFFIT@email.chop.edu)  
**Subject:** RE: Chapter on Vaccine Hesitancy for Vaccines

I suggest that you and Paul discuss this. He has already submitted his new chapter and can best decide where to trim his discussion of vaccine hesitancy and to insert your section. However, we will need this within a month.

Regards,  
Stanley

---

**From:** [Angus.Thomson@sanofipasteur.com](mailto:Angus.Thomson@sanofipasteur.com) [<mailto:Angus.Thomson@sanofipasteur.com>]  
**Sent:** Thursday, September 17, 2015 8:44 AM  
**To:** [stanley.plotkin@vaxconsult.com](mailto:stanley.plotkin@vaxconsult.com); [Stanley.Plotkin@sanofipasteur.com](mailto:Stanley.Plotkin@sanofipasteur.com)  
**Cc:** [Michael.Watson@sanofipasteur.com](mailto:Michael.Watson@sanofipasteur.com); [OFFIT@email.chop.edu](mailto:OFFIT@email.chop.edu)  
**Subject:** RE: Chapter on Vaccine Hesitancy for Vaccines

Stanley,

I can certainly do that – when do you need it on your desk? Thank you for the chance to contribute to this seminal text.

I am not sure how much of the Safety Chapter from the previous edition you are retaining, but there is an emphasis in two sections on the impact of information on behavior and the need to educate parents. The text I have drafted is based on a 5-year program of research and the current literature on the subject (including the SAGE publications), and clearly states that information and education alone have a very limited impact on vaccination behaviours. It also provides an overview of evidence-based approaches to developing social and behavior change interventions.



We will need to just see how to resolve this within the chapter.

Kind regards,

Angus

---

**From:** Stanley Plotkin [<mailto:stanley.plotkin@vaxconsult.com>]  
**Sent:** Wednesday, September 16, 2015 9:29 PM  
**To:** Thomson, Angus (sanofi pasteur); Plotkin, Stanley (sanofi pasteur/EXT)  
**Cc:** Watson, Michael (sanofi pasteur); 'Offit, Paul'  
**Subject:** RE: Chapter on Vaccine Hesitancy for Vaccines

Angus, I just read your excellent article in manuscript. If you can summarize it in 1500 words with 1 or 2 figures that would be OK.

Stanley

---

**From:** [Angus.Thomson@sanofipasteur.com](mailto:Angus.Thomson@sanofipasteur.com) [<mailto:Angus.Thomson@sanofipasteur.com>]  
**Sent:** Tuesday, September 15, 2015 4:19 AM  
**To:** [Stanley.Plotkin@sanofipasteur.com](mailto:Stanley.Plotkin@sanofipasteur.com); [stanley.plotkin@vaxconsult.com](mailto:stanley.plotkin@vaxconsult.com)  
**Cc:** [Michael.Watson@sanofipasteur.com](mailto:Michael.Watson@sanofipasteur.com)  
**Subject:** Chapter on Vaccine Hesitancy for Vaccines

Dear Stanley,

Five years after the MOTIV Think tank in London, it is gratifying to see vaccination acceptance emerge on the international agenda, and to see the research agenda we proposed hold up.

At Sanofi Pasteur we have subsequently developed a broad and collaborative program of R&D, which is now yielding a lot of very robust and informative data (some publications attached).

I recently wrote a book chapter on vaccination acceptance for a Mexican Geriatrics textbook. It is written in English but will be published in Spanish, and is angled slightly towards adult vaccination.

Reviewing Vaccines 6<sup>th</sup> Ed I noted that vaccination acceptance is nested within the Chapter on Vaccine Safety, and finishes with a section on the importance of educating parents. The evidence now clearly shows that education alone will not change perceptions or behaviours. Furthermore, we know now that vaccine hesitancy is not only an issue of vaccine safety; it may stem from beliefs, worldview, or other issues not related to safety. Indeed, in a large 5-country study we have recently found that safety is only a minor barrier to vaccination.

Would you be interested in using this Chapter (attached for your reference) as a backbone to shape a Chapter on Vaccination Acceptance for the next edition of Vaccines? I could work with Paul Offit, and perhaps Bruce Gellin (who was on both the SAGE and NVAC working groups on hesitancy), to fill it out to cover vaccination in general, childhood vaccination, adult vaccination and perhaps adolescent vaccination.

Best regards,

Angus  
Angus Thomson PhD  
Senior Director, Vaccination Policy & Advocacy - Sanofi Pasteur  
2 Ave Pont Pasteur, 69367 Lyon Cedex 7, France  
@ThomsonAngus | tel: + 33 4 37 66 96 86 | cell: + 33 6 71 29 98 50

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**From:** Straus, Walter L.  
**Sent:** Thu, 15 Oct 2015 08:09:06 -0400  
**To:** Destefano, Frank (CDC/OID/NCEZID); Haber, Penina (CDC/OID/NCEZID)  
**Subject:** Personal Update

Hi Frank and Penina,

I wanted to share the good news that I have just taken a new position at Merck, heading up the Clinical Safety and Pharmacovigilance program for Vaccines and Infectious Disease Therapeutics. I am leaving a great job, and taking a new one that is so central to our collective public health mission. It is the job that Fabio recently left, but has broadened a bit in scope.

I am writing both to share the good news, and also to let you know that I have an open position for a medical epidemiologist working in vaccines (and possibly in ID as well). I think it would be a great opportunity for a physician interested in safety who is looking to transition into industry.

So, please feel free to share this information with colleagues. I'm happy also to chat by phone, and this will be easiest once I am back from business travels the end of this month.

Allbest,  
*Walter*

---

**Walter L. Straus, MD, MPH, FCPP, FACP** Executive Director, Global Director for Scientific Affairs / Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 / Fax: 215-616-1095  
Assistant: Betsy Panacio [betsy\\_panacio@merck.com](mailto:betsy_panacio@merck.com) Tel: 267-305-2541

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**From:** Robert Perry  
**Sent:** Wed, 29 Jan 2014 22:40:36 +0000  
**To:** Fisher, Angela H. (CDC/OID/NCEZID) (CTR)  
**Cc:** Tumpey, Abbigail (CDC/OID/NCEZID); Coffin, Nicole (CDC/OID/NCEZID); Dankel, Melissa (CDC/OID/NCEZID); Weinbaum, Cindy (CDC/OID/NCEZID); Destefano, Frank (CDC/OID/NCEZID); Hibbs, Beth (CDC/OID/NCEZID); Miller, Elaine R. (CDC/OID/NCEZID)  
**Subject:** RE: CDC Talking Points re: MMWR Report on Rotavirus Vaccine Administration Errors

Really appreciate the heads up.

**Robert Perry**  
**Dir External Communications**  
Corp Communications  
Global Communications

**GSK**  
5 Crescent Drive, Philadelphia, PA 19112, United States  
**Email** [Robert.P.Perry@gsk.com](mailto:Robert.P.Perry@gsk.com)  
**Tel** +1-407-492-4616

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**From:** Fisher, Angela H. (CDC/OID/NCEZID) (CTR) [mailto:[iwg7@cdc.gov](mailto:iwg7@cdc.gov)]  
**Sent:** Wednesday, January 29, 2014 5:39 PM  
**To:** Robert Perry  
**Cc:** Tumpey, Abbigail (CDC/OID/NCEZID); Coffin, Nicole (CDC/OID/NCEZID); Dankel, Melissa (CDC/OID/NCEZID); Weinbaum, Cindy (CDC/OID/NCEZID); Destefano, Frank (CDC/OID/NCEZID); Hibbs, Beth (CDC/OID/NCEZID); Miller, Elaine R. (CDC/OID/NCEZID)  
**Subject:** CDC Talking Points re: MMWR Report on Rotavirus Vaccine Administration Errors

Good evening, Robert. I hope that you are well. We wanted to touch base to let you know that on Friday, January 31, CDC's *MMWR* will include a "Notes from the Field" that covers rotavirus vaccine administration errors. Attached please find a proof of the piece as well as a copy of our cleared talking points for your review and reference.

Please let us know if you have any questions.

Best,

-Angela

**Angela H. Fisher**  
Health Communications Specialist / Chenega Contractor

Division of Healthcare Quality Promotion (DHQP)  
Centers for Disease Control and Prevention  
1600 Clifton, Bldg. 16, 2113; MS A-07  
Atlanta, GA 30333  
404-639-1665; c) 404-819-4917  
[ahfisher@cdc.gov](mailto:ahfisher@cdc.gov)  
Telework: Tuesdays and Fridays

**From:** Straus, Walter L.  
**Sent:** Thu, 5 Feb 2015 11:36:42 -0500  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: Intro Frank Destefano and Walter Straus

That's great. Would you like for me to call you (if so, what#)? Otherwise, my # is

(b)(6)

Walter

---

Walter L. Straus, MD, MPH, FCPP, FACP Executive Director, Global Director for Scientific Affairs / Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 / Fax: 215-616-1095  
Assistant: Betsy Panacio betsy\_panacio@@merck.com Tel: 267-305-2541

---

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

From: Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
Sent: Thursday, February 05, 2015 8:49 AM  
To: Straus, Walter L.  
Subject: RE: Intro Frank Destefano and Walter Straus

Hi Walter,  
I am available on 2/11 at 4pm.  
Frank

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

From: Straus, Walter L. [[mailto:walter\\_straus@merck.com](mailto:walter_straus@merck.com)]  
Sent: Tuesday, February 03, 2015 2:45 PM  
To: Destefano, Frank (CDC/OID/NCEZID)  
Subject: RE: Intro Frank Destefano and Walter Straus

Frank,  
Do you have a few minutes any of the dates: 2/10, 11 or 12 after 3 PM?

Walter

---

Walter L. Straus, MD, MPH, FCPP, FACP Executive Director, Global Director for Scientific Affairs / Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 / Fax: 215-616-1095  
Assistant: Betsy Panacio betsy\_panacio@@merck.com Tel: 267-305-2541

---

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

From: Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
Sent: Tuesday, February 03, 2015 10:52 AM  
To: Straus, Walter L.  
Subject: RE: Intro Frank Destefano and Walter Straus

CISA is a formal project. It conducts clinical research in addition to providing consultation on individual cases. I'd be happy to discuss further if you like.

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

From: Straus, Walter L. [[mailto:walter\\_straus@merck.com](mailto:walter_straus@merck.com)]  
Sent: Tuesday, February 03, 2015 8:37 AM  
To: Destefano, Frank (CDC/OID/NCEZID)  
Subject: RE: Intro Frank Destefano and Walter Straus

Hi Frank,  
I've had a chance to look at the slides. It's a tremendous help.  
One question I had concerned the CISA project. Is this a formal project, or simply a mechanism for CDC to engage academicians, in an ad hoc manner, on consultations when questions arise regarding safety of a vaccine?  
If easiest, can we find a few minutes to chat by phone?  
Again, MANY thanks. I will, of course, acknowledge you in the presentation.  
Best,

Walter

---

Walter L. Straus, MD, MPH, FCPP, FACP Executive Director, Global Director for Scientific Affairs / Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 /Fax: 215-616-1095  
Assistant: Betsy Panacio [betsy\\_panacio@@merck.com](mailto:betsy_panacio@@merck.com) Tel: 267-305-2541

---

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

From: Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxdl@cdc.gov>]  
Sent: Monday, February 02, 2015 4:29 PM  
To: Straus, Walter L.  
Subject: RE: Intro Frank Destefano and Walter Straus

Hi Walter,  
Good to hear from you. Attached are slides from a general vaccine safety talk that I gave at the NFID Vaccinology course recently. You can borrow at will.  
Best regards,  
Frank

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

From: Straus, Walter L. [[mailto:walter\\_straus@merck.com](mailto:walter_straus@merck.com)]  
Sent: Monday, February 02, 2015 3:42 PM  
To: Chen, Robert (Bob) (CDC/OID/NCHHSTP)  
Cc: Destefano, Frank (CDC/OID/NCEZID)  
Subject: RE: Intro Frank Destefano and Walter Straus

Thanks, Bob.  
I've known Frank for years, but hadn't had a chance to speak recently. Any publicly available slides re VAERS/VSD would be great. We can also easily chat by phone.  
Many thanks to both of you.

Walter

---

Walter L. Straus, MD, MPH, FCPP, FACP Executive Director, Global Director for Scientific Affairs / Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 /Fax: 215-616-1095  
Assistant: Betsy Panacio [betsy\\_panacio@@merck.com](mailto:betsy_panacio@@merck.com) Tel: 267-305-2541

---



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

From: Chen, Robert (Bob) (CDC/OID/NCHHSTP) [<mailto:rtc1@cdc.gov>]  
Sent: Monday, February 02, 2015 3:20 PM  
To: Straus, Walter L.  
Cc: Destefano, Frank (CDC/OID/NCEZID)  
Subject: Intro Frank Destefano and Walter Straus

Walter,

Good to chat. The recent review paper on VSD is PMID: 25108215. There is one on VAERS too but it's still under peer review. So PMID: 15071280 probably best stand in in the interim.

Frank,

Walter Straus (EIS 1990) now at Merck is giving a talk and was wondering if CDC has slides re: VAERS and VSD that he can borrow.

Bob

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

From: Straus, Walter L. [[mailto:walter\\_straus@merck.com](mailto:walter_straus@merck.com)]  
Sent: Monday, February 02, 2015 1:47 PM  
To: Chen, Robert (Bob) (CDC/OID/NCHHSTP)  
Subject: RE: Chat next week?

Bob,

Thanks for this, and for the call.

Best,

Walter

---

Walter L. Straus, MD, MPH, FCPP, FACP Executive Director, Global Director for Scientific Affairs / Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 / Fax: 215-616-1095  
Assistant: Betsy Panacio [betsy\\_panacio@merck.com](mailto:betsy_panacio@merck.com) Tel: 267-305-2541

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**From:** Fernanda Tavares Da Silva  
**Sent:** Tue, 18 Nov 2014 09:56:06 +0000  
**To:** David Vaughn; Broder, Karen (CDC/OID/NCEZID); Valentina Attanasi; François P Roman; Destefano, Frank (CDC/OID/NCEZID); Gronostaj, Michael (CDC/OPHSS/CSELS/DSEPD); Clark, Thomas A. (CDC/ONDIEH/NCCDPHP)  
**Subject:** RE: CDC-GSK Phase 3 and post-licensure PV  
**Attachments:** CDC Ebola vaccine study - draft AEFI\_Prevention Form 11 10 14-3pm1 dv+FT.docx

Dear Karen,  
I also added a couple of comments for consideration.  
Thanks!,  
Best regards,  
Fernanda

---

**From:** David Vaughn  
**Sent:** Monday 17 November 2014 22:05  
**To:** Broder, Karen (CDC/OID/NCEZID); Fernanda Tavares Da Silva; Valentina Attanasi; François P Roman; Destefano, Frank (CDC/OID/NCEZID); Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD)  
**Subject:** RE: CDC-GSK Phase 3 and post-licensure PV

Karen,

See attached or two comments. Talk to you on Thursday. David.

---

**From:** Broder, Karen (CDC/OID/NCEZID) [<mailto:krb2@cdc.gov>]  
**Sent:** Friday, November 14, 2014 11:22 AM  
**To:** David Vaughn; Fernanda Tavares Da Silva; Valentina Attanasi; François P Roman; Destefano, Frank (CDC/OID/NCEZID); Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD)  
**Subject:** RE: CDC-GSK Phase 3 and post-licensure PV

David and Colleagues,

Here is the other draft AEFI prevention form. There is a section in yellow that would be good to update for accuracy re the GSK vaccine.

I am working on getting some schedule info from the CDC folks and will get back to David with some potential times for continued discussion.  
Stay warm.

Thanks,  
Karen

-----Original Appointment-----

**From:** David Vaughn [<mailto:david.w.vaughn@gsk.com>]  
**Sent:** Friday, November 07, 2014 3:26 PM  
**To:** David Vaughn; Fernanda Tavares Da Silva; Valentina Attanasi; François P Roman; Destefano, Frank

(CDC/OID/NCEZID); Gronostaj, Michael (CDC/OID/NCEZID); Broder, Karen (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD)

**Subject:** CDC-GSK Phase 3 and post-licensure PV

**When:** Friday, November 14, 2014 10:00 AM-11:00 AM (UTC-05:00) Eastern Time (US & Canada).

**Where:** TC - see below

When: Friday, November 14, 2014 10:00 AM-11:00 AM (UTC-05:00) Eastern Time (US & Canada).

Where: TC - see below

Note: The GMT offset above does not reflect daylight saving time adjustments.

\*~\*~\*~\*~\*~\*~\*~\*~\*~\*

#### TC Details

Belgium Toll access n: (b)(6)

Belgium Toll-free access n: 0 (b)(6)

Canada Toll access n: +1 (b)(6)

Canada Toll-free access n: 1 (b)(6)

US Toll-free access n: (b)(6)

Participant code: (b)(6)

Registered as GlaxoSmithKline Biologicals SA - Rue de l'Institut, 89 BE-1330 Rixensart – TVA  
BE 0440.872.918 RPM Nivelles. Deutsche Bank AG Bruxelles 826-0006444-59



Ebola Candidate Vaccine Evaluation: Adverse Events Following  
Immunization (AEFI) Prevention Form -- DRAFT

---

(b)(4)

Ebola Candidate Vaccine Evaluation: Adverse Events Following  
Immunization (AEFI) Prevention Form -- DRAFT

---

(b)(4); (b)(5)

Ebola Candidate Vaccine Evaluation: Adverse Events Following  
Immunization (AEFI) Prevention Form -- DRAFT

---

(b)(4); (b)(5)

**From:** Fernanda Tavares Da Silva  
**Sent:** Fri, 7 Nov 2014 20:22:18 +0000  
**To:** David Vaughn  
**Cc:** Broder, Karen (CDC/OID/NCEZID); François P Roman; Gronostaj, Michael (CDC/OPHSS/CSELS/DSEPD); Clark, Thomas A. (CDC/ONDIEH/NCCDPHP); Destefano, Frank (CDC/OID/NCEZID); Valentina Attanasi  
**Subject:** Re: Ebola vaccine pharmacovigilence

I agree :-)  
Fernanda

Sent from my iPhone

On 7 nov. 2014, at 21:18, David Vaughn <[david.w.vaughn@gsk.com](mailto:david.w.vaughn@gsk.com)> wrote:

(b)(5); (b)(4)

---

**From:** Broder, Karen (CDC/OID/NCEZID) [<mailto:krb2@cdc.gov>]  
**Sent:** Friday, November 07, 2014 3:07 PM  
**To:** Fernanda Tavares Da Silva; François P Roman  
**Cc:** David Vaughn; Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); Valentina Attanasi  
**Subject:** RE: Ebola vaccine pharmacovigilence

So to clarify  
If the blood draw is day 0 and 28, is it worth pursuing?

It seems that the issue of lab norms is less important if you have a baseline and post comparison for an individual.

Thanks,

Karen

---

**From:** Fernanda Tavares Da Silva [<mailto:FERNANDA.TAVARES@GSK.COM>]  
**Sent:** Friday, November 07, 2014 3:01 PM  
**To:** François P Roman

**Cc:** Broder, Karen (CDC/OID/NCEZID); David Vaughn; Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); Valentina Attanasi  
**Subject:** Re: Ebola vaccine pharmacovigilence

Dear all,

(b)(5); (b)(4)

Thanks!,  
Fernanda  
Sent from my iPhone

On 7 nov. 2014, at 20:36, François P Roman  
<[FRANCOIS.P.ROMAN@GSK.COM](mailto:FRANCOIS.P.ROMAN@GSK.COM)> wrote:

Dear All,

(b)(4); (b)(5)

Thanks and regards,  
Francois

**François Roman**  
**Director**  
Clinical Research & Translational Science  
Vaccine Discovery & Development

**GSK**  
**89 Rue de l'Institut**  
**Rixensart 1330, Belgium**  
**Email** [FRANCOIS.P.ROMAN@GSK.COM](mailto:FRANCOIS.P.ROMAN@GSK.COM)  
**Mobile** +32 472 900 494  
**Tel** +32 2 656 6738

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---

**From:** Broder, Karen (CDC/OID/NCEZID) [<mailto:krb2@cdc.gov>]  
**Sent:** Friday 7 November 2014 20:32  
**To:** David Vaughn  
**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A.

(CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); François P Roman;  
Fernanda Tavares Da Silva; Valentina Attanasi  
**Subject:** RE: Ebola vaccine pharmacovigilance

David

(b)(5); (b)(4)

Thanks ,

Karen

---

**From:** David Vaughn [<mailto:david.w.vaughn@gsk.com>]  
**Sent:** Friday, November 07, 2014 2:27 PM  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A.  
(CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); François P Roman;  
Fernanda Tavares Da Silva; Valentina Attanasi  
**Subject:** RE: Ebola vaccine pharmacovigilance

Karen,

(b)(5); (b)(4)

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**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A.  
(CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); François P Roman;  
Fernanda Tavares Da Silva; Valentina Attanasi  
**Subject:** RE: Ebola vaccine pharmacovigilance

David,

Thanks a lot; this is very helpful. We were wondering if it would also be possible see the Investigator's brochure or any associated forms?

Also we didn't see any mention of Grade 4 severity in the protocol. Let us know if we missed that

Thanks and have a nice weekend.

Karen

---

**From:** David Vaughn [<mailto:david.w.vaughn@gsk.com>]  
**Sent:** Friday, November 07, 2014 1:37 PM  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); François P Roman; Fernanda Tavares Da Silva; Valentina Attanasi  
**Subject:** RE: Ebola vaccine pharmacovigilence

**Karen,**

Attached you should find the Phase 2 study protocol draft for adults; today's version. It should not be necessary to exceed (or even match) the safety surveillance found in this study for your Phase 3.

**Tom Clark,** Have you received a version of the NIH Phase 3 protocol from Barney Graham?

David.

---

**From:** Broder, Karen (CDC/OID/NCEZID) [<mailto:krb2@cdc.gov>]  
**Sent:** Thursday, November 06, 2014 10:14 AM  
**To:** David Vaughn  
**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: Ebola vaccine pharmacovigilence

Hi David,

I hope you are well. We are working on the vaccine safety sections and forms for the draft CDC Expanded Access protocol for Tom Clark's team. The sections are still evolving as we get input from the staff in the field.

We have been trying to harmonize safety definitions, to the extent practical, with the last version of the NIH protocol we have (Oct 24). Is this the most recent version? Also do you have any of the vaccine safety forms from this study that could be shared with us?



Lastly, we are wondering if it might be helpful to have a short call with you regarding the materials we are developing for safety monitoring, perhaps tomorrow Friday November 7, to get some input?

Thanks,  
Karen

---

**From:** David Vaughn [<mailto:david.w.vaughn@gsk.com>]  
**Sent:** Friday, October 31, 2014 7:06 AM  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Iris De Ryck  
**Subject:** Ebola vaccine pharmacovigilence

Karen,

Do have time next Tuesday or Wednesday to discuss post-marketing (or emergency use) PV in Africa? As the MAH for an Ebola vaccine, we need a Risk Management Plan which includes a PV plan for countries where the vaccine will be used. Capacity building in the affected countries would be challenging. Stand-alone PV studies could be done using sentinel sites. This would all be separate from Phase 3 activities. There is a possibility that GSK will seek EU funding for such efforts and we would like to have an informal discussion with you about what such an effort might look like. If the NIH/GSK vaccine is safe and effective, good PV is of importance to all (including BARDA, CDC, NIH, and DoD) as a bad PV program could derail a good vaccine or identify late a signal that reflects a real problem.

Iris is our clinical safety lead for Ebola vaccine. We are both available Tuesday, 4 November from 0800-0900 and from 1030-1100 and Wednesday 0900-1000 and after 1100 (Iris, recall that Europe falls back on Sunday and so CET is just 5 hours ahead of Philly and Atlanta for a couple weeks).

Thanks, David.

**David W. Vaughn, MD, MPH**  
Head, External R&D, North America  
Vaccines Discovery & Development

**GSK**  
2301 Renaissance Boulevard, RN0220  
King of Prussia, PA 19406-2772, USA  
**Email** [David.W.Vaughn@gsk.com](mailto:David.W.Vaughn@gsk.com)  
**Mobile** +1 267-355-2160  
**Tel** +1 610-787-3907  
**Admin. Support** Elaine Slavish +1 610-787-3102



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**From:** Fernanda Tavares Da Silva  
**Sent:** Fri, 7 Nov 2014 20:21:20 +0000  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** François P Roman; David Vaughn; Gronostaj, Michael (CDC/OPHSS/CSELS/DSEPD); Clark, Thomas A. (CDC/ONDIEH/NCCDPHP); Destefano, Frank (CDC/OID/NCEZID); Valentina Attanasi  
**Subject:** Re: Ebola vaccine pharmacovigilance

Hi Karen,

(b)(5); (b)(4)

Regards,  
Fernanda  
Sent from my iPhone

On 7 nov. 2014, at 21:06, Broder, Karen (CDC/OID/NCEZID) <[krb2@cdc.gov](mailto:krb2@cdc.gov)> wrote:

So to clarify

(b)(5); (b)(4)

Thanks,

Karen

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**To:** François P Roman  
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Dear All,

(b)(4); (b)(5)

weeks to come.

Thanks and regards,  
Francois

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**Director**

Clinical Research & Translational Science

Vaccine Discovery & Development

**GSK**

**89 Rue de l'Institut**

**Rixensart 1330, Belgium**

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**Tel** +32 2 656 6738

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**Sent:** Friday 7 November 2014 20:32

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**Subject:** RE: Ebola vaccine pharmacovigilence

David,

(b)(5); (b)(4)

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Karen

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(b)(4); (b)(5)

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David.

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**Sent:** Thursday, November 06, 2014 10:14 AM  
**To:** David Vaughn  
**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID)  
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Karen

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**From:** David Vaughn [<mailto:david.w.vaughn@gsk.com>]  
**Sent:** Friday, October 31, 2014 7:06 AM  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Iris De Ryck  
**Subject:** Ebola vaccine pharmacovigilence

Karen,



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Thanks, David.

**David W. Vaughn, MD, MPH**

Head, External R&D, North America  
Vaccines Discovery & Development

**GSK**

2301 Renaissance Boulevard, RN0220  
King of Prussia, PA 19406-2772, USA

**Email** [David.W.Vaughn@gsk.com](mailto:David.W.Vaughn@gsk.com)

**Mobile** +1 267-355-2160

**Tel** +1 610-787-3907

**Admin. Support** Elaine Slavish +1 610-787-3102

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BE 0440.872.918 RPM Nivelles. Deutsche Bank AG Bruxelles 826-0006444-59

**From:** David Vaughn  
**Sent:** Fri, 7 Nov 2014 18:37:08 +0000  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Gronostaj, Michael (CDC/OPHSS/CSELS/DSEPD); Clark, Thomas A. (CDC/ONDIEH/NCCDPHP); Destefano, Frank (CDC/OID/NCEZID); François P Roman; Fernanda Tavares Da Silva; Valentina Attanasi  
**Subject:** RE: Ebola vaccine pharmacovigilence  
**Attachments:** 202091 (EBOLA Z CHAD3-005) concept protocol (07-NOV-2014) clean.docx

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Head, External R&D, North America  
Vaccines Discovery & Development

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2301 Renaissance Boulevard, RN0220  
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**Mobile** +1 267-355-2160

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**Admin. Support** Elaine Slavish +1 610-787-3102

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**From:** David Vaughn  
**Sent:** Fri, 31 Oct 2014 17:59:36 +0000  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Iris De Ryck; Destefano, Frank (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID); Gronostaj, Michael (CDC/OPHSS/CSELS/DSEPD); Clark, Thomas A. (CDC/ONDIEH/NCCDPHP); Gargiullo, Paul (CDC/OID/NCIRD)  
**Subject:** RE: Ebola vaccine pharmacovigilence

Thanks. Meeting invitation sent.

---

**From:** Broder, Karen (CDC/OID/NCEZID) [mailto:krb2@cdc.gov]  
**Sent:** Friday, October 31, 2014 1:47 PM  
**To:** David Vaughn  
**Cc:** Iris De Ryck; Destefano, Frank (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID); Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Gargiullo, Paul (CDC/OID/NCIRD)  
**Subject:** RE: Ebola vaccine pharmacovigilence

Hi David and Iris,

Thanks for your invitation to participate in a PV call regarding Ebola Vaccines. The best time on your list is Tuesday November 4 from 8a-9a EST. In addition to me, please invite the other colleagues cced from CDC: Immunization Safety Office - Frank Destefano (ISO director), Tom Shimabukuro, Mike Gronostaj and from the CDC Ebola Response Vaccine Team - Tom Clark and Paul Gargiullo.

Frank reminded me that there is a CIOMS WG on developing recommendations and materials for improving PV (passive and active) in low and middle income countries. Frank (who is serving on that WG) suggested it might also be helpful for Harry Seifert from GSK to be involved in the Ebola vaccine PV discussion call, since he is also on the CIOMS WG. Here is some further information:

[http://www.who.int/vaccine\\_safety/publications/aefi\\_surveillance/en/](http://www.who.int/vaccine_safety/publications/aefi_surveillance/en/)

Have a nice weekend.

Sincerely,

Karen R. Broder, MD  
Captain, United States Public Health Service  
Team Lead  
Clinical Immunization Safety Assessment (CISA) Project  
Immunization Safety Office  
Division of Healthcare Quality Promotion  
Centers for Disease Control and Prevention  
Phone: 404-639-8538 Fax: 404-639-8834  
email: [Kbroder@cdc.gov](mailto:Kbroder@cdc.gov)

---

**From:** David Vaughn [<mailto:david.w.vaughn@gsk.com>]

**Sent:** Friday, October 31, 2014 7:06 AM

**To:** Broder, Karen (CDC/OID/NCEZID)

**Cc:** Iris De Ryck

**Subject:** Ebola vaccine pharmacovigilance

Karen,

(b)(4)

Thanks, David.

**David W. Vaughn, MD, MPH**

Head, External R&D, North America

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Email [David.W.Vaughn@gsk.com](mailto:David.W.Vaughn@gsk.com)

Mobile +1 267-355-2160

Tel +1 610-787-3907

Admin. Support Elaine Slavish +1 610-787-3102

[gsk.com](http://gsk.com) | [Twitter](#) | [YouTube](#) | [Facebook](#) | [Flickr](#)





**From:** Corinne.Jouquelet-Royer@sanofipasteur.com  
**Sent:** Thu, 31 Jul 2014 09:16:17 +0000  
**To:** holmk@cioms.ch; Harry.A.Seifert@gsk.com; Zuber, Patrick (CDC who.int); maurec@who.int; Winiecki, Scott (FDA/CDER); terhi.kilpi@thl.fi; novilia@biofarma.co.id; Destefano, Frank (CDC/OID/NCEZID); liudw929@126.com; Xavier.Kurz@ema.europa.eu; Irina.Caplanusi@ema.europa.eu; Martin, David (FDA/CDER); bergmanu@cioms.ch; Steven.R.Bailey@pfizer.com; dongduo@cdr.gov.cn; BlumM@MedImmune.com  
**Cc:** Francoise.Sillan@sanofipasteur.com; mim [b] (b) (6) [redacted]  
**Subject:** RE: CIOMS WG on VS TG2 chapter 5  
**Attachments:** Safety surveillance Literature search July 2014.docx

Dear all,

As agree you will find attached the result of the literature search. The search criteria included:

Pharmacovigilance

Safety . side effects. Adverse events

Monitoring

Post marketing

Observational study

Vaccine

Surveillance, active surveillance , passive surveillance

Network

LMIC (Low Middle Income Countries)

Feel free to add any reference when writing your section.

Kind regards

Co

---

**From:** Holm Karin [mailto:holmk@cioms.ch]

**Sent:** samedi 5 juillet 2014 21:37

**To:** Jouquelet-Royer, Corinne (sanofi pasteur); Harry.A.Seifert@gsk.com; Patrick Zuber (zuberp@who.int); maurec@who.int; Winiecki, Scott; terhi.kilpi@thl.fi; Bachtar (novilia@biofarma.co.id); fxd1@cdc.gov; Dawei, Liu (liudw929@126.com); Xavier.Kurz@ema.europa.eu; Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu); David.Martin@fda.hhs.gov; Bergman Ulf; Bailey (Steven.R.Bailey@pfizer.com); dongduo@cdr.gov.cn; Blum, Michael (BlumM@MedImmune.com)

**Cc:** Sillan, Francoise (sanofi pasteur); Darko, Mimi (mimidarko66@yahoo.co.uk)

**Subject:** RE: CIOMS WG on VS TG2 chapter 5

Dear Contributors to TG2 Chapter 5,

Additional contributors are needed, especially for section 5.2 and 5.4 --- for the later the public sector is key actor and also a regulator.

For the next TC, I am sending a doodle poll for 1.5 hour on the 8 , 9 or 10 of September in the afternoon.

Please note that Corinne and Harry need your drafts by September 3.

Please note that I am on vacation 7-28 July with only limited access to computers.

Best regards,  
Karin

---

**Karin R. Holm**

Publications Consultant, WG IX Risk Minimisation  
Technical Coordinator, WG on Vaccine Safety  
Council for International Organizations of Medical Sciences (CIOMS)  
Associate partner of UNESCO and in official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Ofc Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)

---

**From:** Holm Karin

**Sent:** 05 July 2014 21:33

**To:** Jouquelet-Royer, Corinne; [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); Patrick Zuber ([zuberp@who.int](mailto:zuberp@who.int)); [maurec@who.int](mailto:maurec@who.int); Winiecki, Scott; [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); Bachtar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); [Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu); Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; Bailey ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com)); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com))

**Cc:** [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); Darko, Mimi ([mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk))

**Subject:** RE: CIOMS WG on VS TG2 chapter 5

Dear Contributors to TG2 Chapter 5,

---

**Karin R. Holm**

Publications Consultant, WG IX Risk Minimisation  
Technical Coordinator, WG on Vaccine Safety  
Council for International Organizations of Medical Sciences (CIOMS)  
Associate partner of UNESCO and in official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Ofc Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)

---

**From:** Holm Karin

**Sent:** 24 June 2014 11:36

**To:** Jouquelet-Royer, Corinne; [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); Patrick Zuber ([zuberp@who.int](mailto:zuberp@who.int)); [maurec@who.int](mailto:maurec@who.int); Winiecki, Scott; [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); Bachtar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); [Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu); Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; Bailey ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com))

**Cc:** [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); Darko, Mimi ([mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk))

**Subject:** CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon (French time)

Dear CIOMS TG2 Chapter 5 Contributors,

Corinne Jouquelet-Royer (Sanofi, who is new to the CIOMS WG but will eventually take over at some point in the future for Françoise, who is moving to a new area at Sanofi) and Harry Seifert (GSK) kindly

offered to organize Chapter 5 of the Manual on Active Safety Surveillance. Ch.5 is the “meat of the manual” on Establishing Active Surveillance (see Table of Contents in business plan draft attached).

The best day/time was this Friday, 27 June, 12pm French time. Sanofi kindly will arrange TC and send instructions on how to access.

#### Agenda for TC

- Quick review of the section 5 to get alignment and shared understanding on what need to be achieved
- Agree on contributors to which sections
- And timelines for draft and reviews before September meeting

	June 2014
	Fri 27
	12:00 PM
Karin Holm	NO
corinne jouquelet royer	OK
Harry Seifert	OK
Patrick Zuber	OK
Christine Maure	OK
Scott Winiecki (FDA)	OK
Frank DeStefano	NO
Terhi Kilpi	OK
Novilia Sjafri Bachtar	OK
Xavier Kurz	OK
Dawei Liu	?
Irina Caplanusi	?
David Martin	?
Steven Bailey	?
Ulf Bergman	NO
Count	8

#### Karin R. Holm

Technical Coordinator, Working Group on Vaccine Safety  
 Publications Consultant, Working Group IX Risk Minimization  
 Council for International Organizations of Medical Sciences (CIOMS)  
 Associate partner of UNESCO / In official relations with WHO  
 c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
 Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
 Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)



---

**From:** Holm Karin  
**Sent:** 23 June 2014 16:05  
**To:** 'Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com))'; 'Bachtiar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id))'; 'Xavier.Kurz@ema.europa.eu'; 'Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu))'; 'David.Martin@fda.hhs.gov'; 'terhi.kilpi@thl.fi'; Bergman Ulf  
**Cc:** 'Jouquelet-Royer, Corinne'; 'Francoise.Sillan@sanofipasteur.com'; 'Darko, Mimi' (b)(6)  
**Subject:** RE: Doodle: Link for poll "CIOMS WG on VS TG2 section 5"

*Dear Dawei Liu, Novi, Xavier, Irina, David, Terhi, Ulf...*  
*We haven't yet heard from you if you are available at these times and we are trying to find the best time for a TC to work on Section 5 of the Manual on Active Safety Surveillance....*

Hi, CIOMS WG on VS - TG2 Active Surveillance section 5

Corinne Jouquelet-Royer and Harry Seifert would like to have a TC to start the process moving on drafting section 5. Please let us know if you would be available any of these times by clicking on this doodle poll...

<http://doodle.com/b6z8aicfaia92fbt>

Thank you,  
Karin

Most popular date: Friday, June 27, 2014 12:00 PM |

	Top of Form		
	<b>June 2014</b>		<b>July 2014</b>
<b>7 participants</b>	<b>Fri 27</b>	<b>Tue 1</b>	<b>Wed 2</b>
	<b>12:00 PM</b>	<b>5:00 PM</b>	<b>6:00 PM</b>
Karin Holm		✓	
corinne jouquelet	✓	✓	✓
royer			
Harry Seifert	✓	✓	✓
Patrick Zuber	✓		
Christine Maure	✓		
Scott Winiecki	✓		✓
Frank DeStefano			
	Friday, June 27, 2014	Tuesday, July 1, 2014	Wednesday, July 2, 2014
	12:00 PM	5:00 PM	6:00 PM
	Bottom of Form		

\*\*\*\*\*  
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**To:** Françoise Sillan, Corinne  
Jouquelet-Royer

**From:** Anne-Céline Eydan

Request date: July 8, 2014

Delivery date: July 23, 2014

**Subject: Safety surveillance: Observational Studies**

Search strategy

## Embase Session Results (23 Jul 2014)

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#6	#1 AND #5
#5	'vaccine'/exp/dd_ae
#1	'observational study'/exp

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## Low & Middle Income Countries

### **Children who received PCV-10 vaccine from a two-dose vial without preservative are not more likely to develop injection site abscess compared with those who received pentavalent (DPT-HepB-Hib) vaccine: A longitudinal multi-site study**

[Berhane Y.](#), [Worku A.](#), [Demissie M.](#), [Tesfaye N.](#), [Asefa N.](#), [Aniemaw W.](#), [Weldearegawi B.](#), [Kebede Y.](#), [Shiferaw T.](#), [Worku A.](#), [Olijira L.](#), [Merdekios B.](#), [Ashebir Y.](#), [Tadesse T.](#), [Dessie Y.](#), [Meseret S.](#), [Ayele G.](#)

PLoS ONE 2014 9:6 Article Number e97376

Go to publisher for the [full text](#)

**Background:** The single dose pneumonia ten-valent vaccine has been widely used and is highly efficacious against selected strains *Streptococcus pneumoniae*. A two-dose vial without preservative is being introduced in developing countries to reduce the cost of the vaccine. In routine settings improper immunization practice could result in microbial contamination leading to adverse events following immunization. **Objective:** To monitor adverse events following immunization recommended for routine administration during infancy by comparing the rate of injection-site abscess between children who received PCV-10 vaccine and children who received the Pentavalent (DPT-HepB-Hib) vaccine. **Methods:** A longitudinal population-based multi-site observational study was conducted between September 2011 and October 2012. The study was conducted in four existing Health and Demographic Surveillance sites run by public universities of Abraminch, Haramaya, Gondar and Mekelle. Adverse events following Immunization were monitored by trained data collectors. Children were identified at the time of vaccination and followed at home at 48 hour and 7 day following immunization. Incidence of abscess and relative risk with the corresponding 95% Confidence Intervals were calculated to examine the risk



difference in the comparison groups. Results: A total of 55, 268 PCV and 37, 480 Pentavalent (DPT-HepB-Hib) vaccinations were observed. A total of 19 adverse events following immunization, 10 abscesses and 9 deaths, were observed during the one year study period. The risk of developing abscess was not statistically different between children who received PCV-10 vaccine and those received Pentavalent (RR = 2.7, 95% CI 0.576-12.770), and between children who received the first aliquot of PCV and those received the second aliquot of PCV (RR = 1.72, 95% CI 0.485-6.091). Conclusion: No significant increase in the risk of injection site abscess was observed between the injection sites of PCV-10 vaccine from a two-dose vial without preservative and pentavalent (DPT-HepB-Hib) vaccine in the first 7 days following vaccination. © 2014 Berhane et al.

**A prospective observational safety study on MF59® adjuvanted cell culture-derived vaccine, Celtura® during the A/H1N1 (2009) influenza pandemic**

[Reynales H.](#), [Astudillo P.](#), [de Vallière S.](#), [Hatz C.](#), [Schlagenhauf P.](#), [Rath B.](#), [Velentgas P.](#), [Fariña A.](#), [Sales-Carmona V.](#), [Groth N.](#)

**Vaccine** 2012 **30:45** (6436-6443)

Go to publisher for the [full text](#)

Background: The present study was a prospective observational study to evaluate the safety profile of Celtura®, a monovalent, cell culture-derived, inactivated subunit influenza vaccine prepared from A/California/07/2009(H1N1) with the adjuvant MF59®. Subjects were enrolled prospectively during the H1N1 2009 influenza pandemic at medical centres in **Colombia, Chile, Switzerland, and Germany** during the period December 2009 to June 2010. Methods: Subjects ages 18 and older were followed for the occurrence of adverse events (AEs) for six months after vaccination. Adverse events of special interest (AESIs) were neuritis, convulsion (seizure), anaphylaxis, encephalitis, vasculitis, Guillain-Barre syndrome, demyelinating conditions, Bell's palsy, and laboratory-confirmed vaccination failure. Results: Overall, 7348 AEs were reported in 2296 of 3989 enrolled subjects (57.6%). Only two AEs were considered related to injection site reactions. No laboratory-confirmed cases of influenza were reported. There were 108 medically confirmed serious adverse events (SAEs) reported among 73 subjects with 6 such SAEs described as possibly or probably related to vaccination. Three fatal cases were reported and assessed as not related to vaccination. Two AESIs classified as convulsion were reported and assessed as not related to vaccination. Both AESIs occurred well outside the pre-specified 7 day risk window representing the likely timeframe of the occurrence of seizure following vaccination. Conclusions: The results of this study support the overall good safety profile of MF59 adjuvanted cell culture-derived influenza vaccine as administered in adults during the 2009-2010 H1N1 influenza pandemic. No concern is raised regarding the occurrence of AESIs. © 2012 Elsevier Ltd.

**Safety observation of influenza a H1N1 influenza vaccine vaccinations in 3300 medical workers**

[He X.-L.](#), [Kang S.-Q.](#), [Gong C.-Y.](#), [Jiang G.-Y.](#)



Objective: To investigate safety of influenza A H1N1 vaccine vaccinations.

Methods: A total of 3 300 medical workers were vaccinated by batch of 200909012 influenza A H1N1 vaccine produced by Shanghai Biological Products Corporation Limited according to the principle of voluntary and concentration. The adverse reactions were observed within half an hour, three days and a week after vaccinations, respectively. Results: The inoculators with local or systemic reaction reached 1.18% (39/3 300). There were 0.15% (5/3 300) of the inoculators with adverse reaction within half an hour; 0.70% (23/3 300) within 1 to 3 days after vaccination; and 0.33% (11/3 300) within 3 days to 1 week after vaccination. No severe adverse events were found. Conclusion: Influenza A H1N1 vaccine vaccinations is an economic and effective way of influenza A H1N1 prevention with mild reactions. © 2010 Editorial Board of Chin J Evid-based Med.

### **Active assessment of adverse events following yellow fever vaccination of persons aged 60 years and more**

[Miyaji K.T.](#), [Luiz A.M.](#), [Lara A.N.](#), [Chaves T.D.S.S.](#), [Piorelli R.D.O.](#), [Lopes M.H.](#), [Sartori A.M.C.](#)

**Human Vaccines and Immunotherapeutics** 2013 **9:2** (277-282)

Go to publisher for the [full text](#)

Introduction: Older age has been associated to serious adverse events (AE) following yellow fever (YF) vaccination in passive surveillance studies, but few prospective studies involving seniors have been published. Results: Nine hundred and six persons were evaluated; 78 were not vaccinated and 828 received the vaccine; 700 (84.7%) were interviewed after vaccination: 593 (84.7%) did not report any symptoms or signs following YF vaccine; 107 (15.3%) reported at least one AE temporally associated to YF vaccination: 97 (13.9%) had systemic AE and 17 (2.4%) reported AE at the injection site (7 had both systemic and local AE). Data regarding previous vaccination was available for 655 subjects. Statistically significant higher rates of systemic AE were observed among subjects who received the first YF vaccination (17.5%) in comparison to persons who had been previously vaccinated (9.5%). Methods: This observational prospective study aimed to describe AE following YF vaccination in persons aged  $\geq 60$  y. From March 2009 to April 2010, seniors who sought YF vaccination at a reference Immunization Center in **Sao Paulo city, c Brazil**, were included. Demographic and clinical data, previous YF vaccination, travel destination and the final decision regarding YF vaccination or not were collected from standardized medical records. Active AE assessment was done through telephone or electronic mail interview performed approximately 14 d after immunization. Conclusion: Most persons aged  $\geq 60$  y may be safely vaccinated against YF. Before vaccination, they must be carefully screened for conditions associated to altered immunocompetence and for risk of exposure to YF. © 2013 Landes Bioscience.



## Long-term follow-up observation of the safety, immunogenicity, and effectiveness of Gardasil™ in adult women

[Luna J.](#), [Plata M.](#), [Gonzalez M.](#), [Correa A.](#), [Maldonado I.](#), [Nossa C.](#), [Radley D.](#), [Vuocolo S.](#), [Haupt R.M.](#), [Saah A.](#)

**PLoS ONE** 2013 **8:12** Article Number e83431

Go to publisher for the [full text](#)

Background: Previous analyses from a randomized trial in women aged 24-45 have shown the quadrivalent HPV vaccine to be efficacious in the prevention of infection, cervical intraepithelial neoplasia (CIN) and external genital lesions (EGL) related to HPV 6/11/16/18 through 4 years. In this report we present long term follow-up data on the efficacy, safety and immunogenicity of the quadrivalent HPV vaccine in adult women. Methods: Follow-up data are from a study being conducted in 5 sites in **Colombia** designed to evaluate the long-term immunogenicity, effectiveness, and safety of the qHPV vaccine in women who were vaccinated at 24 to 45 years of age (in the original vaccine group during the base study [n = 684]) or 29 to 50 years of age (in the original placebo group during the base study [n = 651]). This analysis summarizes data collected as of the year 6 post-vaccination visit relative to day 1 of the base study (median follow-up of 6.26 years) from both the original base study and the Colombian follow-up. Results: There were no cases of HPV 6/11/16/18-related CIN or EGL during the extended follow-up phase in the per-protocol population. Immunogenicity persists against vaccine-related HPV types, and no evidence of HPV type replacement has been observed. No new serious adverse experiences have been reported. Conclusions: Vaccination with qHPV vaccine provides generally safe and effective protection from HPV 6-, 11-, 16-, and 18-related genital warts and cervical dysplasia through 6 years following administration to 24-45 year-old women. Trial Registration: Clinicaltrials.gov NCT00090220 © 2013 Luna et al.

## Post-authorization safety surveillance of a liquid pentavalent vaccine in Guatemalan children

[Asturias E.J.](#), [Contreras-Roldan I.L.](#), [Ram M.](#), [Garcia-Melgar A.J.](#), [Morales-Oquendo V.](#), [Hartman K.](#), [Rauscher M.](#), [Moulton L.H.](#), [Halsey N.A.](#)

**Vaccine** 2013 **31:49** (5909-5914)

Go to publisher for the [full text](#)

Objective: Combination vaccines have improved the efficiency of delivery of new vaccines in low and middle-income countries. Post-authorization monitoring of adverse events (AEs) after vaccination with a liquid pentavalent DTwP-HepB-Hib combination vaccine was conducted in Guatemalan infants. Methods: A prospective observational safety study of the incidence of medical attended events (MAEs) and serious adverse events (SAEs) in children who received pentavalent and oral polio vaccines at 2, 4 and 6 months of age was conducted in two clinics at the Institute of Guatemala. Parents were contacted by telephone after each dose. All outpatient, emergency department visits, and hospitalizations were monitored. A self-controlled analysis was conducted to determine if there was evidence of increased risk of MAEs or SAEs following vaccines as compared to control time windows. Results: Of 3000 recruited infants, 2812 (93.7%) completed the third dose and 2805 (93.5%) completed follow-up. Ten AEs in eight infants, of which four SAEs in four infants, were classified as related to the vaccine. Thirteen deaths were reported due to



common illnesses of infancy, and none were judged to be related to the vaccine. The mortality rate (4.4 per 1000) was lower than expected for the population. The incidence-rate-ratio for healthcare visits was lower in post-vaccination time windows than for control windows; after the first vaccine dose, the rate ratios for the risk periods of 0-1, 2-6, and 7-30 days post-vaccination were 0.3, 0.5, and 0.7, respectively (all statistically significantly different from the reference value of 1.0 for the 31-60 day control period). Conclusion: The liquid pentavalent vaccine was associated with lower rates of health care visits and not associated with increases in SAEs or hospitalizations. Systems can be set up in low to middle income countries to capture all health care visits to monitor the safety of new vaccines. © 2013 Elsevier Ltd.

### **Long-term follow-up of study participants from prophylactic HIV vaccine clinical trials in Africa**

[Schmidt C.](#), [Jaoko W.](#), [Omota-Manyonyi G.](#), [Kaleebu P.](#), [Mpendo J.](#), [Nanvubya A.](#), [Karita E.](#), [Bayingana R.](#), [Bekker L.-G.](#), [Chomba E.](#), [Kilembe W.](#), [Nchabeleng M.](#), [Nyombayire J.](#), [Stevens G.](#), [Chetty P.](#), [Lehrman J.](#), [Cox J.](#), [Allen S.](#), [Dally L.](#), [Smith C.](#), [Fast P.E.](#)

**Human Vaccines and Immunotherapeutics** 2014 **10:3** (714-723)

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Long-term safety is critical for the development and later use of a vaccine to prevent HIV/AIDS. Likewise, the persistence of vaccine-induced antibodies and their impact on HIV testing must be established. IAVI has sponsored several Phase I and IIA HIV vaccine trials enrolling healthy, HIV-seronegative African volunteers. Plasmid DNA and viral vector based vaccines were tested. No vaccine-related serious adverse events were reported. After completion of vaccine trials conducted between 2001-2007, both vaccine and placebo recipients were offered enrolment into an observational long-term follow-up study (LTFU) to monitor potential late health effects and persistence of immune responses. At scheduled 6-monthly clinic visits, a health questionnaire was administered; clinical events were recorded and graded for severity. Blood was drawn for HIV testing and cellular immune assays. 287 volunteers were enrolled; total follow-up after last vaccination was 1463 person years (median: 5.2 years). Ninety-three (93)% of volunteers reported good health at their last LTFU visit. Infectious diseases and injuries accounted for almost 50% of the 175 reported clinical events, of which over 95% were mild or moderate in severity. There were 30 six pregnancies, six incident HIV infections and 14 volunteers reported cases of social harm. Persistence of immune responses was rare. No safety signal was identified. No potentially vaccine-related medical condition, no immune mediated disease, or malignancy was reported. HIV vaccines studied in these trials had a low potential of induction of persisting HIV antibodies. © 2014 Landes Bioscience.

### **Other countries**



## **Prospective safety monitoring of Haemophilus influenzae type b and heptavalent pneumococcal conjugate vaccines in Kagoshima, Japan**

[Nishi J.](#), [Tokuda K.](#), [Imuta N.](#), [Minami T.](#), [Kawano Y.](#)

**Japanese Journal of Infectious Diseases** 2013 **66:3** (235-237)

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Haemophilus influenzae type b (Hib) conjugate vaccine (PRP-T) and heptavalent pneumococcal conjugate vaccine (PCV7) were introduced in Japan in December 2008 and February 2010, respectively. The concurrent administration of these vaccines is routinely performed worldwide. However, the safety of the simultaneous administration of these vaccines has not been fully evaluated in Japan, because it has rarely been performed thus far. We conducted a 2-year prospective, observational, multicenter study on PRP-T and PCV7 safety from February 2009 through January 2011 in 29 facilities located in Kagoshima Prefecture, Japan. Objective severe adverse events included anaphylactoid reaction, encephalitis/encephalopathy, neurological events, severe focal reactions, systemic eruption/urticaria, fever above 39.9°C within 2 days after inoculation, and other complications requiring hospitalization. The incidences of these events for PRP-T and PCV7 administration were 0.68% (76/11,197) and 0.92% (28/3,049), respectively. No deaths or subsequent complications were reported during the course of the study. There was no significant difference in the incidence of severe adverse events between the single and co-administration groups for both vaccines: PRP-T, 0.55% (31/5,662) versus 0.81% (45/5,535;  $P = 0.11$ ); PCV7, 0.88% (11/1,247) versus 0.94% (17/1,802;  $P = 0.86$ ). These results suggest that the simultaneous administration of vaccines including PRP-T and/or PCV7 does not increase the incidence of severe adverse events in Japanese children.

## **Monitoring adverse events of the vaccination campaign against influenza A (H1N1) in the Netherlands**

[Van Puijenbroek E.P.](#), [Broos N.](#), [Van Grootheest K.](#)

**Drug Safety** 2010 **33:12** (1097-1108)

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Background: In November 2009, a vaccination campaign against Influenza A (H1N1) was started in the Netherlands. The accelerated registration procedure of the vaccines used in this campaign and the use of these vaccines on a large scale indicated a need for real-time safety monitoring. Objective: To describe the processing, analysing and performing of signal detection by the Netherlands Pharmacovigilance Centre (Lareb) on reports of adverse events following immunization (AEFI) with respect to the two pandemic influenza vaccines, Focetria® and Pandemrix®, used in the Netherlands. The secondary aim is to provide a summary of the results of the safety monitoring of both vaccines. Study Design: Description of the process of collecting information and analysis of the safety monitoring of the pandemic vaccines during the vaccination campaign against H1N1 in the Netherlands. An observational study on adverse events following immunization (AEFIs) associated with vaccines used in this campaign was conducted. Results: The use of a dedicated web form with predefined AEFIs enabled an efficient way of processing and analysing the reports, resulting in a close to real-time monitoring of the safety of the vaccines. From 1 November 2009 until 1 March 2010, 7534 reports concerning one or more AEFIs possibly related to the administration of both vaccines were



received. 2788 of the reports related to Focetria® and 4746 of the reports related to Pandemrix®. The total time between receiving the reports and completion was longer for the serious reports (average 2.8 days) compared with the non-serious reports (average 0.8 days). The profile of the reported adverse events is comparable with the information provided in the Summary of Product Characteristics (SPC). Differences in reported AEFIs between both vaccines may be caused by bias and confounding due to the different populations for which these vaccines have been used. No signals of possible batch-related problems were detected for either vaccine. © 2010 Adis Data Information BV. All rights reserved.

### **Safety of Zostavax™-A cohort study in a managed care organization**

[Baxter R.](#), [Tran T.N.](#), [Hansen J.](#), [Emery M.](#), [Fireman B.](#), [Bartlett J.](#), [Lewis N.](#), [Saddier P.](#)

**Vaccine** 2012 **30:47** (6636-6641)

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Background: Zostavax™ is a live, attenuated varicella-zoster virus vaccine indicated for the prevention of herpes zoster (shingles). An observational post-licensure (Phase IV) study was conducted at Kaiser Permanente Northern California (KPNC), a US managed care organization, to assess the safety of zoster vaccine in people 60 years of age or older, vaccinated in routine medical care. Methods: We performed a cohort study, comparing rates of clinical events resulting in hospitalizations or emergency department visits in a 42-day risk time period immediately following vaccination with rates in the same cohort in a subsequent comparison time period. The study data were reviewed and interpreted by an external safety review committee of 3 independent experts. Results: Approximately 29,000 people ≥ 60 years of age were vaccinated with zoster vaccine from July 2006 to November 2007. Of the 386 comparisons performed for the main analysis, 4 had an increased relative risk with a nominal p-value. ≤ 0.05. After medical records review, the timing of these conditions and procedures was found to be often prior to vaccination, and no clear increase in health events was observed in the risk period following vaccination compared to later. Persons receiving zoster vaccine appeared to be in their optimal health at the time of vaccination, which led to an apparent protective effect of the vaccine for some health outcomes, due to the study design. Conclusions: There was no evidence of a safety concern for zoster vaccine. © 2012 Elsevier Ltd.

### **An early (3-6 weeks) active surveillance study to assess the safety of pandemic influenza vaccine Focetria® in a province of Emilia-Romagna region, Italy - Part One**

[Candela S.](#), [Pergolizzi S.](#), [Ragni P.](#), [Cavuto S.](#), [Nobilio L.](#), [Di Mario S.](#), [Dragosevic V.](#), [Groth N.](#), [Magrini N.](#)

**Vaccine** 2013 **31:10** (1431-1437)

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Introduction: An observational, non-comparative, prospective, surveillance study of individuals vaccinated with the MF59-adjuvanted A/H1N1 influenza vaccine, Focetria®, (Novartis Vaccines & Diagnostics, Siena, Italy), was



performed in Italy during the 2009 A/H1N1 influenza pandemic. Method: This study assessed the short-term (six-week) safety profile of the investigational vaccine in real time. After vaccination (N= 7943), adverse events (AE) were assessed using both active (telephone) and passive (healthcare database) follow-up in enrolled vaccinated subjects, including infants (6-23 months), pregnant women, and the immunosuppressed. The treating physicians of all subjects experiencing AEs post-vaccination were consulted for clinical information on the conditions reported. All AEs were coded according to ICD-10. Results: A total of 1583 AEs occurred during the study, 67 (4.2%) of which were serious adverse events (SAEs). One SAE was considered to be possibly related to vaccination (transitory and ill-defined neurologic disorder experienced by a 16-year-old asthmatic male). Three adverse events of special interest (AESI) were identified (convulsions experienced by two epileptic subjects), none of which were considered to be vaccine-related. Six individuals died during the study period, in each case the cause of death was not related to vaccination (four cases of severe underlying co-morbidity, one case of psychoactive drug misuse, and one case of acute myocardial infarction). Conclusions: No cases of clinically relevant AEs, SAEs, or AESI were observed within a six-week period of vaccine administration. In accordance with existing clinical and post-marketing safety data, the results of this active surveillance study demonstrate a good safety profile for the MF59-adjuvanted A/H1N1 vaccine, Focetria, within the general population. © 2012 Elsevier Ltd.

### **Safety of AS03-adjuvanted split-virion H1N1 (2009) pandemic influenza vaccine: A prospective cohort study**

[Nazareth I.](#), [Tavares F.](#), [Rosillon D.](#), [Haguinet F.](#), [Bauchau V.](#)

**BMJ Open** 2013 **3:2** Article Number 001912

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Objectives: To assess the safety of an AS03- adjuvanted split virion H1N1 (2009) vaccine (Pandemrix) in persons vaccinated during the national pandemic influenza vaccination campaign in the UK. Design: Prospective, cohort, observational, postauthorisation safety study. Setting: 87 general practices forming part of the Medical Research Council General Practice Research Framework and widely distributed throughout England. Participants: A cohort of 9143 individuals aged 7 months to 97 years who received at least one dose of the AS03-adjuvanted H1N1 pandemic vaccine during the national pandemic influenza vaccination campaign in the UK was enrolled. 94% completed the 6-month follow-up. Exclusion criteria were previous vaccination with other H1N1 pandemic vaccine and any child in care. Primary and secondary outcome measures: Medically attended adverse events (MAEs) occurring within 31 days after any dose, serious adverse events (SAEs) and adverse events of special interest (AESIs) following vaccination were collected for all participants. Solicited adverse events (AEs) were assessed in a subset of participants. Results: MAEs were reported in 1219 participants and SAEs in 113 participants during the 31-day postvaccination period. The most frequently reported MAEs and SAEs were consistent with events expected to be reported during the winter season in this population: lower respiratory tract infections, asthma and pneumonia. The most commonly reported solicited AEs were irritability in young children aged <5 years (61.8%), muscle aches in children aged 5-17 years (61.9%) and adults (46.9%). 18 AESIs, experienced by 14 patients, met the



criteria to be considered for the observed-to-expected analyses. AESIs above the expected number were neuritis (1 case within 31 days) and convulsions (8 cases within 181 days). There were 41 deaths during the 181-day period after vaccination, fewer than expected. Conclusions: Results indicate that the AS03-adjuvanted H1N1 pandemic vaccine showed a clinically acceptable reactogenicity and safety profile in all age and risk groups studied.

**A postlicensure evaluation of the safety of Ann Arbor strain live attenuated influenza vaccine in children 24-59 months of age**

[Toback S.L.](#), [Ambrose C.S.](#), [Eaton A.](#), [Hansen J.](#), [Aukes L.](#), [Lewis N.](#), [Wu X.](#), [Baxter R.](#)

**Vaccine** 2013 **31:14** (1812-1818)

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Background: In the **United States**, live attenuated influenza vaccine (LAIV) was initially approved for use in individuals aged 5-49 years in 2003, which was extended to individuals aged 2-49 years in 2007. At that time, a postlicensure commitment was made to describe the safety of LAIV within a cohort of eligible children aged 2-5 years. Methods: A prospective observational postmarketing study was conducted to evaluate the safety of LAIV. Rates of medically attended events (MAEs) and serious adverse events (SAEs) in eligible children aged 24-59 months receiving LAIV as part of routine care from October 2007 to March 2010 were compared with rates in a within-cohort self-control, as well as matched unvaccinated and matched trivalent inactivated influenza vaccine (TIV)-vaccinated controls. Children with asthma and other high-risk medical conditions before vaccination were excluded. All MAEs and SAEs through 42 days postvaccination and all hospitalizations and deaths through 6 months postvaccination were analyzed. Statistical significance was declared without multiplicity adjustment. Results: A total of 28,226 unique LAIV recipients were matched with similar numbers of TIV-vaccinated and unvaccinated children. Of 4696 MAE incidence rate comparisons, 83 (1.8%) were statistically significantly higher and 221 (4.7%) were statistically significantly lower in LAIV recipients versus controls. No pattern of MAE rate differences suggested a safety signal with LAIV. Asthma/wheezing MAEs were not statistically increased in LAIV recipients. No anaphylaxis events occurred within 3 days postvaccination. Rates of SAEs were similar between LAIV and control groups. Conclusions: Results of this postlicensure evaluation of LAIV safety in US children are consistent with preapproval clinical studies and Vaccine Adverse Event Reporting System reports, both of which demonstrated no significant increase in asthma/wheezing events or other adverse outcomes among eligible children aged 24-59 months who received LAIV. © 2013 Elsevier Ltd.

**Post-marketing safety evaluation of a tetanus toxoid, reduced diphtheria toxoid and 3-component acellular pertussis vaccine administered to a cohort of adolescents in a united states health maintenance organization**

[Klein N.P.](#), [Hansen J.](#), [Lewis E.](#), [Lyon L.](#), [Nguyen B.](#), [Black S.](#), [Weston W.M.](#), [Wu S.](#), [Li P.](#), [Howe B.](#), [Friedland L.R.](#)

**Pediatric Infectious Disease Journal** 2010 **29:7** (613-617)



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**Background:** Prelicensure clinical studies may not include sufficient numbers of subjects to assess the potential for rare postvaccination adverse events. The aim of this postlicensure study (NCT00297856) was to evaluate uncommon outcomes following vaccination with a tetanus, reduced-antigen-content diphtheria, and acellular pertussis vaccine (Tdap, Boostrix GlaxoSmithKline) in a large adolescent cohort. **Methods:** We monitored safety outcomes among 13,427 10 to 18-year-old adolescents enrolled in the Northern California Kaiser Permanente Health Care Plan who received Tdap vaccination as part of their normal health care. Subjects were evaluated using self-control analysis comparing days 0 to 29 to days 30 to 59 postvaccination for neurologic events, hematologic events and allergic reactions. We evaluated new onset chronic illnesses within 6 months of Tdap vaccination by comparing with historical Td controls matched for age at vaccination, season, sex, and geographic area. We also compared the incidence of events of interest between the Tdap and historical cohorts as exploratory analyses. **Results:** No increased risk for medically attended neurologic (odds ratio [OR], 0.962; 95% confidence interval [CI], 0.533-1.733) or allergic reactions (OR, 1.091; 95% CI, 0.441-2.729) was observed following Tdap vaccination when comparing the first 30 postvaccination days to the second 30 postvaccination days. There was one hematologic event within 30 days of Tdap, compared with 0 events within days 30 to 59 ( $P = 1.0$ ). When compared with matched historical Td recipients, no increase in new onset chronic illnesses (OR, 0.634; 95% CI, 0.475-0.840) was seen after Tdap. No deaths occurred in the Tdap cohort during the study. **Conclusions:** This study provides no evidence for an increased risk for neurologic, hematologic, allergic events, or new onset of chronic illnesses among adolescents vaccinated with Tdap. © 2010 by Lippincott Williams & Wilkins.

**Adverse events associated with pandemic influenza vaccines:  
Comparison of the results of a follow-up study with those coming from  
spontaneous reporting**

[Carvajal A.](#), [Ortega P.G.](#), [Sáinz M.](#), [Velasco V.](#), [Salado I.](#), [Martín Arias L.H.](#),  
[Eiros J.M.](#), [Pérez Rubio A.](#), [Castrodeza J.](#)

**Vaccine** 2011 **29:3** (519-522)

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Prior to marketing of pandemic influenza vaccines, the only safety data were those from clinical trials. The objective of this study was to compare information coming from spontaneous reporting with that systematically collected in a formal observation study; this also permits to further evaluate safety of pandemic influenza vaccines in the targeted patients' population. Out of a sample of 507 vaccinated subjects, 103 (20.3%) developed some complication. In the same period 83 reports corresponding to all vaccinated people of **Castilla y León** ( $n=131,462$ ) were collected. Severe cases were 1 (1%) and 7 (8.4%), respectively, with the two procedures. The spontaneous reporting rate was 322-fold lower than that identified through the follow-up study; when considered the severe cases, it was 37-fold lower. Under certain circumstances reporting might be performing better than usual due to strengthening of the surveillance system. Adverse events observed for the pandemic H1N1 vaccines lie within the expected safety profile for common



events with influenza vaccines. An overall benefit-risk assessment of these vaccines should be done. © 2010.

### **Observational safety study of febrile convulsion following first dose MMRV vaccination in a managed care setting**

[Jacobsen S.J.](#), [Ackerson B.K.](#), [Sy L.S.](#), [Tran T.N.](#), [Jones T.L.](#), [Yao J.F.](#), [Xie F.](#), [Craig Cheetham T.](#), [Saddier P.](#)

**Vaccine** 2009 **27:34** (4656-4661)

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Background: A combined measles, mumps, rubella, varicella live vaccine (MMRV, Merck and Co., Inc., US) was recently licensed in **the US**. Pre-licensure clinical trial data showed a significant increase in fever in days 5-12 following MMRV vaccination as compared to the vaccines given separately (MMR + V). This post-licensure retrospective cohort study was undertaken to assess the incidence of febrile convulsion following MMRV. Methods: Children ages 12-60 months who received a first dose of MMRV in February 2006-June 2007 in a managed care organization were included in the study. Subjects were optimally matched on age, sex, and calendar date of vaccination to children who received MMR + V concomitantly in November 2003-January 2006, before MMRV licensure. Potential cases of febrile convulsion were identified through administrative data and adjudicated by expert panel, according to pre-specified criteria. Results: During the 30 days post-vaccination, there were 128 and 94 potential convulsion cases among the 31,298 children in the MMRV and MMR + V cohorts, respectively. After review of available medical charts and adjudication, there were 84 cases of confirmed febrile convulsion, 44 (1.41/1000) and 40 (1.28/1000) in the MMRV and MMR + V cohorts, respectively (RR = 1.10, 95% CI = 0.72, 1.69). In days 5-12 following vaccination, a pre-specified period of interest, the respective numbers were 22 (0.70/1000) and 10 (0.32/1000) (RR = 2.20, 95% CI = 1.04, 4.65). Conclusion: These data suggest that the risk of febrile convulsion is increased in days 5-12 following vaccination with MMRV as compared to MMR + V given separately during the same visit, when post-vaccination fever and rash are also increased in clinical trials. While there was no evidence of an increase in the overall month following vaccination, the elevated risk during this time period should be communicated and needs to be balanced with the potential benefit of a combined vaccine. © 2009 Elsevier Ltd. All rights reserved.

### **U.S. Postlicensure safety surveillance for adolescent and adult tetanus, diphtheria and acellular pertussis vaccines: 2005-2007**

[Chang S.](#), [O'Connor P.M.](#), [Slade B.A.](#), [Woo E.J.](#)

**Vaccine** 2013 **31:10** (1447-1452)

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Background: Pre-licensure clinical trials for two U.S. licensed tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccines did not reveal any major safety concerns. However, routine use in large adolescent and adult populations could reveal rare and potentially serious adverse events (AEs). Methods: To characterize reported AEs following Tdap vaccination and identify potential safety concerns warranting further evaluation, we analyzed data from



the Vaccine Adverse Event Reporting System (VAERS) and assessed the frequency and proportions of AEs and reporting rates (reports per 100,000 vaccine doses distributed). Results: A total of 2090 reports (7% were serious; 55% listed Tdap alone) involving Tdap vaccines were submitted to VAERS May 2005-June 2007. The crude reporting rate was 10.2 per 100,000 vaccine doses distributed. The median age of vaccinees was 22 years, and the female to male ratio was about 2 to 1. The majority of reports described common local and systemic signs and symptoms, such as injection site reactions, fever, and headache. Rarely reported AEs included myopericarditis, demyelinating diseases of the central nervous system, Guillain-Barré Syndrome, syncope, encephalopathy/encephalitis, seizure, Bell's palsy, anaphylaxis, and thrombocytopenia. Conclusions: Because adolescents and adults were not routinely vaccinated against pertussis in the past, this surveillance summary provides important - and reassuring - information about the use of Tdap in these age groups. Although subject to the limitations of passive surveillance, the findings of this VAERS review support the pre-licensure clinical trial data with regard to the safety of the U.S. licensed Tdap vaccines. Continued monitoring of clinically significant AEs that are temporally associated with Tdap vaccination and further assessment of such events using controlled observational studies may provide additional information about the safety of these vaccines. © 2012.

**Immunogenicity and safety of the bivalent HPV vaccine in female patients with juvenile idiopathic arthritis: A prospective controlled observational cohort study**

[Heijstek M.W.](#), [Scherpenisse M.](#), [Groot N.](#), [Tacke C.](#), [Schepp R.M.](#), [Buisman A.-M.](#), [Berbers G.A.M.](#), [Van Der Klis F.R.M.](#), [Wulffraat N.M.](#)

**Annals of the Rheumatic Diseases** 2014 **73:8** (1500-1507)

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Objectives: To compare the immunogenicity and safety of the bivalent human papillomavirus (HPV)16/18 vaccine between female patients with juvenile idiopathic arthritis (JIA) and healthy female adolescents. Methods: 68 patients and 55 healthy girls aged 12-18 years were included in a prospective controlled observational cohort and were vaccinated at 0, 1 and 6 months. Primary outcomes were immunogenicity expressed as seropositivity rate after three vaccine doses at 7 and 12 months and HPV-specific geometric mean antibody concentrations. Secondary outcomes were HPV16/18-specific memory B cell responses in a subset of participants and safety, defined as adverse events and the effect of vaccination on JIA disease activity. Results: All participants were seropositive for HPV16 and HPV18 at 7 months. One patient turned seronegative at 12 months for HPV16/18. No significant differences were found between patients and controls in HPV-specific antibody concentrations; however, antibody concentrations were consistently lower in patients. No effect of methotrexate on HPV16 antibodies ( $p=0.79$ ) or HPV18 antibodies ( $p=0.37$ ) was detected. All patients on anti-TNF $\alpha$  treatment were seropositive after vaccination. The kinetics of HPV16/18 memory B cell responses was comparable between patients and controls, but the magnitude of B cell responses at 7 and 12 months appeared lower in patients. No relevant differences in adverse events were found. HPV vaccination did not aggravate JIA disease. Conclusions: The bivalent HPV16/18 vaccine is immunogenic and well tolerated in JIA



patients. However, HPV-specific antibodies and B cell responses tended to be lower in patients compared with healthy controls.

## General articles

### **Use of the self-controlled case-series method in vaccine safety studies: Review and recommendations for best practice**

[Weldeselassie Y.G.](#), [Whitaker H.J.](#), [Farrington C.P.](#)

**Epidemiology and Infection** 2011 **139:12** (1805-1817)

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The self-controlled case-series method was originally developed to investigate potential associations between vaccines and adverse events, and is now commonly used for this purpose. This study reviews applications of the method to vaccine safety investigations in the period 1995-2010. In total, 40 studies were reviewed. The application of the self-controlled case-series method in these studies is critically examined, with particular reference to the definition of observation and risk periods, control of confounders, assumptions and potential biases, methodological and presentation issues, power and sample size, and software. Comparisons with other study designs undertaken in the papers reviewed are also highlighted. Some recommendations are presented, with the emphasis on promoting good practice. © 2011 Cambridge University Press.

### **Registration of observational studies: Is it time?**

[Williams R.J.](#), [Tse T.](#), [Harlan W.R.](#), [Zarin D.A.](#)

**CMAJ** 2010 **182:15** (1638-1642)

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Observational studies form an important part of the medical evidence base, particularly for assessing rare adverse events and long-term effectiveness of medications and devices. 1 However, observational studies, like interventional studies (clinical trials), are subject to publication bias and reporting bias. 2–4 Registration of clinical trials is a widely recognized tool for facilitating complete public reporting. 5 Registration of observational studies has received less attention, although interest is growing. 6–8 Because existing registries (e.g., ClinicalTrials.gov) accommodate observational studies, and the rationale and benefits of registration are similar, we ask the scientific community and other stakeholders to consider the systematic, prospective registration of observational studies.

### **A scan statistic for identifying optimal risk windows in vaccine safety studies using self-controlled case series design**

[Xu S.](#), [Hambidge S.J.](#), [Mcclure D.L.](#), [Daley M.F.](#), [Glanz J.M.](#)

**Statistics in Medicine** 2013 **32:19** (3290-3299)

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In the examination of the association between vaccines and rare adverse events after vaccination in postlicensure observational studies, it is challenging to define appropriate risk windows because prelicensure RCTs provide little insight on the timing of specific adverse events. Past vaccine safety studies have often used prespecified risk windows based on prior publications, biological understanding of the vaccine, and expert opinion. Recently, a data-driven approach was developed to identify appropriate risk windows for vaccine safety studies that use the self-controlled case series design. This approach employs both the maximum incidence rate ratio and the linear relation between the estimated incidence rate ratio and the inverse of average person time at risk, given a specified risk window. In this paper, we present a scan statistic that can identify appropriate risk windows in vaccine safety studies using the self-controlled case series design while taking into account the dependence of time intervals within an individual and while adjusting for time-varying covariates such as age and seasonality. This approach uses the maximum likelihood ratio test based on fixed-effects models, which has been used for analyzing data from self-controlled case series design in addition to conditional Poisson models. © 2013 John Wiley & Sons, Ltd.

### **Monitoring and assessing vaccine safety: A European perspective**

[Lopalco P.L.](#), [Johansen K.](#), [Ciancio B.](#), [De Carvalho Gomes H.](#), [Kramarz P.](#), [Giesecke J.](#)

**Expert Review of Vaccines** 2010 **9:4** (371-380)

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The success of vaccination programs is an uncontroversial reality - in Europe as well as worldwide. On the other hand, the perceived risk of adverse events in the general public is the most important threat for implementing successful vaccination programs in Europe. For this reason, monitoring and assessing vaccine safety is a priority for public health. Vaccine safety is assessed both before and after vaccine authorization. In postmarketing settings, different activities related to vaccine safety usually involve several different stakeholders. In 2005, a new EU agency, the European Centre for Disease Prevention and Control, was established with the aim to strengthen Europe's defences against infectious diseases. Implementing stable links between different stakeholders and defining clear roles in the EU is paramount in order to provide optimal and transparent information on adverse reactions following immunization, with the final goal of increasing compliance to safe and effective vaccination programs. © 2010 Expert Reviews Ltd.

### **A study of adverse drug reactions in patients admitted to intensive care unit of a tertiary care teaching rural hospital**

[Kathiria J.M.](#), [Sattigeri B.M.](#), [Desai P.M.](#), [Patel S.P.](#)

**International Journal of Pharmacy and Pharmaceutical Sciences** 2013 **5:1** (160-163)

Adverse drug reactions (ADRs) are the common problems faced in the setups like ICU where the poly pharmacy is involved in treating the patients. Control of such events is possible if the culpable drug is known or if it is identified and



reported. However, reporting of adverse drug reactions still remains in its infancy for problems in many. Awareness about adverse drug reactions can decrease irrational use of medicines, poly pharmacy and adverse drug-drug interactions. A prospective, observational and non-interventional study was conducted over a period of 18 months in medical ICU of Dhiraj hospital, Piparia with the goal to highlight the responsibility of health care professionals in preventing, identifying, diagnosis, treating and reporting ADRs. The patients were monitored daily for ADRs. The data was analyzed for demographic parameters. The causality relationship between suspected drugs and the reactions were assessed by using various standard causality assessment scales. 1000 patients were enrolled for the study. Out of these 45 patients developed ADRs. Of these 27 males and 18 females developed ADRs showing male predominance (2. 7%). The ADRs increased with increasing number of drugs administered. The drug class most commonly implicated with ADRs was antibiotics 24(53. 33%). The system most commonly involved with an ADR was gastrointestinal tract 26. 67%. Most commonly reported reaction were hypoglycemia (13. 33%) and Rash (11. 11%).

## Pregnancy

### **H1N1 influenza vaccination during pregnancy**

[Fell D.B.](#), [Dodds L.](#), [McNeil S.](#), [MacDonald N.E.](#)

**BMJ (Online)** 2014 **348** Article Number g3500

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H1N1 safety data look reassuring, but we need ongoing surveillance of all influenza vaccines given to pregnant women

Risks to pregnant women from influenza infection have long been recognized.<sup>1</sup> The recent 2009-10 H1N1 pandemic was no exception—pregnant women were at higher risk of severe H1N1 influenza illness compared with the general population,<sup>2</sup> and those with H1N1 influenza had higher rates of adverse pregnancy outcomes than did uninfected pregnant women.<sup>3</sup> Despite limited safety data for use of the monovalent H1N1 vaccines in pregnancy, pregnant women were widely prioritized for H1N1 vaccination programs.<sup>4</sup> Fortunately, enhanced surveillance of pregnant women during the pandemic has enabled retrospective evaluation of the safety of monovalent H1N1 vaccine in obstetric populations around the world.

### **Influenza H1N1 vaccination and adverse pregnancy outcome**

[Ludvigsson J.F.](#), [Zugna D.](#), [Cnattingius S.](#), [Richiardi L.](#), [Ekblom A.](#), [Örtqvist Å.](#), [Persson I.](#), [Stephansson O.](#)

**European Journal of Epidemiology** 2013 **28:7** (579-588)

Go to publisher for the [full text](#)

Although vaccines against influenza can reduce maternal morbidity and mortality, large-scale data on adverse effects in the offspring are scarce.



Historical cohort study in Stockholm County, Sweden. We linked H1N1 vaccination data (Pandemrix®, a mono-valent AS03 adjuvanted H1N1 vaccine) with pregnancy and birth data from 21,087 women with singleton offspring conceived between February 2009 and January 2010 (vaccinated during pregnancy: n = 13,297 vs. unvaccinated: n = 7,790). Data were analysed by conceptualizing the observational cohort as a series of nested cohorts defined at each week of gestation. Logistic regression estimated odds ratios (ORs) for low birth weight (LBW, <2,500 g), preterm birth (<37 completed weeks), small-for-gestational age (SGA, <10th percentile of the gestational age-specific birth weight within the cohort), low 5-min Apgar score (<7), and caesarean section. Data were adjusted for potential confounders, including maternal age, body mass index, smoking, parity, civil status and comorbidities. Compared with infants of non-vaccinated women, infants of vaccinated women had similar adjusted ORs (95 % CI) for LBW (0.91; 0.79-1.04), preterm birth (0.99; 0.89-1.10), SGA (0.97; 0.90-1.05), low Apgar score (1.05, 0.84-1.31), and a marginal risk reduction for caesarean section (0.94, 0.89-0.99). H1N1 vaccination during pregnancy, using an AS03-adjuvanted vaccine, does not appear to adversely influence offspring risks of LBW, preterm birth, SGA, or low Apgar score. Our results suggest that this vaccine is safe for the offspring when used in different stages of pregnancy. © 2013 Springer Science+Business Media Dordrecht.

**Influenza H1N1 (swine flu) vaccination: A safety surveillance feasibility study using self-reporting of serious adverse events and pregnancy outcomes**

[Mackenzie I.S.](#), [Macdonald T.M.](#), [Shakir S.](#), [Dryburgh M.](#), [Mantay B.J.](#), [Mcdonnell P.](#), [Layton D.](#)

**British Journal of Clinical Pharmacology** 2012 **73:5** (801-811)

Go to publisher for the [full text](#)

**Aims:** During the global H1N1 influenza A (swine flu) pandemic 2009-2010, swine flu vaccines were expeditiously licensed and a mass vaccination programme for high risk groups, including pregnant women, was introduced in the UK. This pilot active safety surveillance study was performed to establish the feasibility of rapidly monitoring the new swine flu vaccines in large patient numbers receiving or offered the vaccination under normal conditions of use within a short time frame. **Methods:** A cohort design with safety data capture through modern technologies was carried out in Scotland, UK during the winter swine flu vaccination programme 2009-2010 in individuals receiving or offered the swine flu vaccination. The main outcome measures were self-reported serious adverse events (SAEs) and pregnancy outcomes. **Results:** The cohort comprised 4066 people; 3754 vaccinated and 312 offered the vaccination but not vaccinated. There were 939 self-reported events (838 different events), 53 judged to fit SAE criteria by the investigators, with nine judged as possibly, probably or definitely vaccine related. None of the seven deaths (six in vaccinees) were judged as vaccine related. One hundred and twenty-eight women reported 130 pregnancies during the study with 117 pregnant at study start. There were reports of four miscarriages in three women and six possible congenital abnormalities in live births. **Conclusions:** Overall, no significant safety issues were identified. The methodology and use of modern technologies to collect safety data from large numbers of patients was successful and could



be used again in similar safety studies. © 2011 The Authors. British Journal of Clinical Pharmacology © 2011 The British Pharmacological Society.

### **A(H1N1)v2009: A controlled observational prospective cohort study on vaccine safety in pregnancy**

[Oppermann M.](#), [Fritzsche J.](#), [Weber-Schoendorfer C.](#), [Keller-Stanislawski B.](#), [Allignol A.](#), [Meister R.](#), [Schaefer C.](#)

**Vaccine** 2012 **30:30** (4445-4452)

Go to publisher for the [full text](#)

Background: A(H1N1)v2009 influenza vaccination of pregnant women was a challenge for health care providers, as little safety data were available. Methods: We prospectively followed the pregnancies of women who were vaccinated at any time during pregnancy or  $\leq 4$  weeks prior to conception and compared these outcomes to a control cohort matched by the estimated date of birth. Primary endpoints: rate of spontaneous abortion and major malformations. Secondary endpoints: preeclampsia, gestational age at birth, and birth weight. Results: Pregnancy outcome of 323 women immunized with adjuvanted or non-adjuvanted A(H1N1)v2009 influenza vaccines from 2009-09-28 to 2010-03-31 were compared to 1329 control subjects. The risk for spontaneous abortions (HR 0.89; 95% CI 0.36-2.19) and the rate of major malformations (all trimesters: OR 0.87; 95% CI 0.38-1.77; preconception and first trimester exposure: OR 0.79; 95% CI 0.13-2.64) did not vary between the two cohorts. Furthermore, there was no increase in preeclampsia, prematurity, and intrauterine growth retardation in the vaccinated cohort. Conclusion: The results of our study do not indicate a risk for the pregnant woman and the developing embryo/fetus after H1N1 vaccination. We provide and apply methods novel in observational studies on pregnancy outcome, especially if a single dose exposure is investigated. © 2012 Elsevier Ltd.

### **Maternal safety of trivalent inactivated influenza vaccine in pregnant women**

[Nordin J.D.](#), [Kharbanda E.O.](#), [Benitez G.V.](#), [Nichol K.](#), [Lipkind H.](#), [Naleway A.](#), [Lee G.M.](#), [Hambidge S.](#), [Shi W.](#), [Olsen A.](#)

**Obstetrics and Gynecology** 2013 **121:3** (519-525)

Go to publisher for the [full text](#)

OBJECTIVE: To estimate the risks for medically attended events occurring within 42 days of receiving trivalent inactivated influenza vaccine and to evaluate specific risks of first-trimester vaccination. METHODS: This retrospective observational cohort study compared rates of medically attended adverse events in trivalent inactivated influenza-vaccinated and unvaccinated pregnant women in the Vaccine Safety Datalink. Using a Poisson distribution and log link, we calculated maternal adjusted incident rate ratios for composite safety outcomes for the full cohort and the subset vaccinated during the first trimester. RESULTS: The cohort included 75,906 vaccinated (28.4% in the first trimester) and 147,992 unvaccinated women matched by age, site, and pregnancy start date. In the first 3 days after vaccination, trivalent inactivated influenza vaccine was not associated with increased risk of specified medically attended events, including allergic reactions, cellulitis, and seizures (full cohort



adjusted incident rate ratio 1.12, 95% confidence interval [CI] 0.81-1.55; P=.48; first-trimester adjusted incident rate ratio .97, 95% CI 0.53-1.78; P=.93). In the first 42 days, no incident cases of Guillain-Barré syndrome, optic neuritis, transverse myelitis, or Bells palsy were identified. Trivalent inactivated influenza vaccine was not associated with thrombocytopenia (full cohort adjusted incident rate ratio 0.90, 95% CI 0.68-1.19; P=.45; first-trimester adjusted incident rate ratio 0.56, 95% CI 0.22-1.39; P=.21) or an acute neurologic event (full cohort adjusted incident rate ratio 0.92, 95% CI 0.54-1.6; P=.75; first-trimester adjusted incident rate ratio 1.05, 95% CI 0.46-2.38; P=.91). **CONCLUSIONS:** Receipt of trivalent inactivated influenza vaccine during pregnancy was not associated with increased risk of adverse events in the 42 days after vaccination, supporting its safety for the mother. © 2013 by The American College of Obstetricians and Gynecologists.

### **Safety of seasonal influenza and influenza A (H1N1) 2009 monovalent vaccines in pregnancy**

[Moro P.L.](#), [Tepper N.K.](#), [Grohskopf L.A.](#), [Vellozzi C.](#), [Broder K.](#)

**Expert Review of Vaccines** 2012 **11:8** (911-921)

Go to publisher for the [full text](#)

Inactivated influenza vaccines have been given to pregnant women since 1964. Since 2004, the Advisory Committee on Immunization Practices has recommended that pregnant women receive trivalent inactivated influenza vaccine at any time during pregnancy. Studies conducted before 2009 did not identify any safety concerns after trivalent inactivated influenza vaccine in mothers or their infants. During the 2009-2010 influenza A (H1N1) influenza vaccination program, several monitoring systems were established or enhanced to assess whether adverse events were associated with H1N1 2009 monovalent vaccines (2009 H1N1 influenza vaccines). Data from these systems did not identify any safety concerns in pregnant women who received 2009 H1N1 influenza vaccines or their infants. Although live attenuated influenza vaccines are not recommended in pregnant women, a small number of studies have not shown any safety concern among pregnant women or their infants who were inadvertently exposed to these vaccines. This review summarizes US and international safety data for influenza vaccines in pregnant women with an emphasis on 2009 H1N1 influenza vaccines. © 2012 2012 Expert Reviews Ltd.

### **Safety of MF59-adjuvanted A/H1N1 influenza vaccine in pregnancy: A comparative cohort study**

[Heikkinen T.](#), [Young J.](#), [Van Beek E.](#), [Franke H.](#), [Verstraeten T.](#), [Weil J.G.](#), [Della Cioppa G.](#)

**American Journal of Obstetrics and Gynecology** 2012 **207:3** (177.e1-177.e8)

Go to publisher for the [full text](#)

Objective: The 2009-2010 A/H1N1 pandemic provided a unique setting to study the safety of MF59-adjuvanted vaccination in pregnancy. Study Design: This was an observational cohort study of the safety of an MF59-adjuvanted A/H1N1 vaccine (Focetria) conducted among 4508 pregnant women (2295 vaccinated vs 2213 unvaccinated), with 3 month follow-up of neonates. Results: No maternal



deaths or abortions occurred among the vaccinated women. No differences between the vaccinated and unvaccinated cohorts were observed for gestational diabetes, preeclampsia, stillbirth, low birthweight, neonatal deaths, or congenital malformations. The risk of premature birth was significantly decreased among the vaccinated women (adjusted proportional hazard, 0.69; 95% confidence interval, 0.51-0.92). No differences were observed in rates of congenital malformations after vaccination in the first (2.1%), second (2.7%), or third (2.1%) trimesters. Conclusion: There was no evidence of a safety risk for MF59-adjuvanted A/H1N1 vaccination in pregnant women; protection was observed against premature birth. © 2012 Mosby, Inc.

**Pharmacovigilance monitoring of a cohort of pregnant women vaccinated against influenza A(H1N1) variant virus in the Nord-Pas de Calais region of northern France**

[Auffret M.](#), [Béné J.](#), [Gautier S.](#), [Moreau-Crépeaux S.](#), [Caron J.](#)

**European Journal of Obstetrics Gynecology and Reproductive Biology** 2013 **170:1** (114-118)

Go to publisher for the [full text](#)

**Objective** During the 2009-2010 influenza A variant virus (A(H1N1)v) pandemic in France, a national pharmacovigilance program was set up to monitor vaccinated, pregnant women, especially the reactogenicity of the vaccine and its impact on the outcome of pregnancy and on the newborn. Here, we present the results for the cohort of pregnant women constituted in the Nord-Pas de Calais region of northern France. **Study design** Vaccinated pregnant women were included in the study by the region's vaccination centers between November 2009 and April 2010. **Results** Eight hundred and six pregnant women were included and 781 were followed up until delivery. The risk of adverse events after vaccination and the maternal, fetal and neonatal medical conditions in our cohort did not appear different from the risk observed in the general population. **Conclusions** Our results suggest that A(H1N1)v vaccination of pregnant women did not have an adverse

## **Epidemiology study**

**Prevalence of cervical human papillomavirus infection and types among women immigrated to Sicily, Italy**

[Giovannelli L.](#), [Vassallo R.](#), [Matranga D.](#), [Affronti M.](#), [Caleca M.P.](#), [Bellavia C.](#), [Perino A.](#), [Ammatuna P.](#)

**Acta Obstetricia et Gynecologica Scandinavica** 2009 **88:6** (737-742)

Go to publisher for the [full text](#)

We determined the prevalence of human papillomavirus (HPV) cervical infection and HPV genotypes among 115 women immigrating to Sicily (Italy), with regard to abnormal cytology and socio-behavioral characteristics in a cross-sectional, observational study. Information was collected with the help of cultural mediators/translators. HPV-DNA was assayed by the INNOLiPA HPV



assay and a nested PCR/sequencing method. Sixty (52.2%) women came from sub-Saharan Africa and 55 (47.8%) from Eastern Europe. HPV infection was found in 55 (47.8%) women. The most frequent types were the oncogenic types HPV-16 (7.8%), HPV-18 and 51 (6.0% each), HPV-52 (5.2%), 31, 53, and 68 (4.3% each). Twenty-seven (23.5%) women had cytological abnormalities associated with HPV infection ( $p=0.04$ ). Being single (OR = 2.98; 95%CI: 1.30-6.84) and parity (OR = 0.29; 95%CI: 0.12-0.65) were consistent predictors of HPV infection. Only 21 (18.2%) women returned to collect the results of their Pap and HPV tests. The high prevalence of HPV infection and oncogenic types among immigrant women make them a priority group for cervical cancer screening. Linguistically and culturally appropriate prevention efforts are needed to sensitize immigrant women regarding HPV-related issues and to conduct vaccine strategies for cervical cancer prevention.

### **Epidemiology of rotavirus gastroenteritis among children under 5 years of age in Tunisia - Results of sentinel hospital surveillance 2009 to 2011**

[Soltani M.](#), [Bouanene I.](#), [Trabelsi A.](#), [Harbi A.](#), [Hachicha M.](#), [Amri F.](#), [Boussnina S.](#), [Gueddiche M.N.](#), [Sfar M.T.](#), [Teleb N.](#), [Ben Ghorbel M.](#), [Ben Hamida E.](#)

**Revue d'Epidemiologie et de Sante Publique** 2012 **60:6** (473-480)

Go to publisher for the [full text](#)

Background: Rotavirus is the major cause of severe acute gastroenteritis among young children. The objectives of this study were to assess the epidemiology, clinical and virological features of community-acquired rotavirus acute gastroenteritis, in children under 5 years of age, hospitalized in Tunisia. Methods: A multicenter prospective observational study was conducted from April 2009 to March 2011, in 11 sentinel pediatric departments. Clinical data and stool samples were collected for all children under 5 years, admitted for acute gastroenteritis. Rotavirus was detected by Elisa immunoassay test and genotyped for G and P by semi-nested multiplex RT-PCR. Result: A total of 621 children were enrolled in this study. Rotavirus was detected in 30.3% of cases (95% CI [26.7-33.9]). The estimated incidence rate of rotavirus acute gastroenteritis was 11 cases/100,000 child-years (95% CI [9.43-12.57]). This infection affected predominantly children aged under 24 months, and occurred mainly in winter (55.3%). Vomiting, fever and dehydration were observed in 79.6%, 69.5% and 57% respectively. Genotype analysis identified four G types (G1, G2, G3 and G4) and 4 P types (P[4], P[6], P[8] and P[9]). The most common G/P combination was G3P[8] (24.4%), followed by G4P[8] (13.3%) and G1P[8] (6.5%). Conclusion: These results highlight the frequency and potential severity of rotavirus acute gastroenteritis in pediatric hospital settings. The present study could provide a sufficient database to make a decision related to the introduction of rotavirus vaccine in Tunisian national immunization program. © 2012 Elsevier Masson SAS.

### **Epidemiology of HPV in HIV-positive and HIV-negative fertile women in cameroon, West Africa**

[Desruisseau A.J.](#), [Schmidt-Grimminger D.](#), [Welty E.](#)

Go to publisher for the [full text](#)

**Background.** HPV types vary by country and HIV status. There are no data on the prevalent HPV genotypes from Cameroon. **Methods.** We conducted a cross-sectional, observational study on 65 Cameroonian women. Samples were sent for HPV genotyping and Thin Prep analyses. **Results.** 41 out of 61 samples tested (67.2) had HPV subtypes detected. The most common high risk types encountered were: 45 (24.6) and 58 (21.5). HIV-positive women were more likely to test positive for any HPV ( $P=.014$ ), have more than one HPV subtype ( $P=.003$ ), and to test positive for the high risk subtypes ( $P=.007$ ). Of those with high risk HPV, HIV-positive women were more likely to have Thin Prep abnormalities than HIV-negative women ( $P=.013$ ). **Conclusions.** Oncogenic HPV subtypes 45 and 58 were more prevalent than those subtypes carried in the quadrivalent vaccine. Further studies are needed to assess whether the current vaccine will be effective in this region. © 2009 Andrew J. Desruisseau et al.



**From:** Corinne.Jouquelet-Royer@sanofipasteur.com  
**Sent:** Mon, 30 Jun 2014 12:12:46 +0000  
**To:** holmk@cioms.ch; Harry.A.Seifert@gsk.com; Zuber, Patrick (CDC who.int); maurec@who.int; Winiecki, Scott (FDA/CDER); terhi.kilpi@thl.fi; novilia@biofarma.co.id; Destefano, Frank (CDC/OID/NCEZID); liudw929@126.com; Xavier.Kurz@ema.europa.eu; Irina.Caplanusi@ema.europa.eu; Martin, David (FDA/CDER); bergmanu@cioms.ch; Steven.R.Bailey@pfizer.com; Ayman.Ayoub@pfizer.com; BlumM@MedImmune.com  
**Cc:** Francoise.Sillan@sanofipasteur.com; (b)(6); bergmanu@cioms.ch  
**Subject:** RE: CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon- notes and call for contributor  
**Attachments:** TG2 TC Section 5 June 27.pptx

Dear all,

Please find the updated slides from your meeting last week.

**We need more contributors: feel free to contact me or Karin .**

Don't hesitate to comments or add if I missed or misunderstood anything.

Best regards

Corinne

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** mardi 24 juin 2014 17:36  
**To:** Jouquelet-Royer, Corinne (sanofi pasteur); 'Harry.A.Seifert@gsk.com'; 'Patrick Zuber (zuberp@who.int)'; 'maurec@who.int'; 'Winiecki, Scott'; 'terhi.kilpi@thl.fi'; 'Bachtiar (novilia@biofarma.co.id)'; 'fxd1@cdc.gov'; 'Dawei, Liu (liudw929@126.com)'; 'Xavier.Kurz@ema.europa.eu'; 'Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu)'; 'David.Martin@fda.hhs.gov'; Bergman Ulf; 'Bailey (Steven.R.Bailey@pfizer.com)'; Ayman.Ayoub@pfizer.com  
**Cc:** Sillan, Francoise (sanofi pasteur); 'Darko, Mimi (b)(6)'; Bergman Ulf  
**Subject:** RE: CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon (French time)

Dear CIOMS TG2 section 5 Contributors:

Corinne and Harry are looking forward to talking with you on: **Fri 27 June 12noon (French time)**

Attached please find the latest version of the business plan (including the Manual Table of Contents) for discussion.

#### Agenda for TC

- Quick review of the section 5 to get alignment and shared understanding on what need to be achieved
- Agree on contributors to which sections
- And timelines for draft and reviews before September meeting

#### Sanofi Telecon dial in numbers

France	(b)(6)	(local)
Canada	(b)(6)	(local)

US : (b)(6)  
Belgique (b)(6)  
Singapore - (b)(6)  
Mexique - (b)(6)

Participant code (b)(6)  
Code PIN (CP) : (b)(6)

Additional Numbers can be found here: <http://www.intercall.com/sanofi/numbers/index.htm>

Wishing you good connections and hope all try to speak clearly, loudly, slowly for optimal communication!

Karin

**Karin R. Holm**

Technical Coordinator, Working Group on Vaccine Safety  
Publications Consultant, Working Group IX Risk Minimization  
Council for International Organizations of Medical Sciences (CIOMS)  
Associate partner of UNESCO / In official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

---

**From:** Holm Karin

**Sent:** 24 June 2014 11:36

**To:** Jouquelet-Royer, Corinne; [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); Patrick Zuber ([zuberp@who.int](mailto:zuberp@who.int)); [maurec@who.int](mailto:maurec@who.int); Winiecki, Scott; [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); Bachtiar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); [Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu); Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; Bailey ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com))

**Cc:** [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); Darko, Mimi (b)(6)

**Subject:** CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon (French time)

Dear CIOMS TG2 Chapter 5 Contributors,

Corinne Jouquelet-Royer (Sanofi, who is new to the CIOMS WG but will eventually take over at some point in the future for Françoise, who is moving to a new area at Sanofi) and Harry Seifert (GSK) kindly offered to organize Chapter 5 of the Manual on Active Safety Surveillance. Ch.5 is the "meat of the manual" on Establishing Active Surveillance (see Table of Contents in business plan draft attached).

The best day/time was this Friday, 27 June, 12pm French time. Sanofi kindly will arrange TC and send instructions on how to access.

**Agenda for TC**

- Quick review of the section 5 to get alignment and shared understanding on what need to be achieved
- Agree on contributors to which sections
- And timelines for draft and reviews before September meeting

June 2014

	Fri 27
	12:00 PM
Karin Holm	NO
corinne jouquelet royer	OK
Harry Seifert	OK
Patrick Zuber	OK
Christine Maure	OK
Scott Winiecki (FDA)	OK
Frank DeStefano	NO
Terhi Kilpi	OK
Novilia Sjafri Bachtar	OK
Xavier Kurz	OK
Dawei Liu	?
Irina Caplanusi	?
David Martin	?
Ayman Ayoub	?
Steven Bailey	NO
Ulf Bergman	NO
Count	8

**Karin R. Holm**

Technical Coordinator, Working Group on Vaccine Safety  
Publications Consultant, Working Group IX Risk Minimization  
Council for International Organizations of Medical Sciences (CIOMS)  
Associate partner of UNESCO / In official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)

---

**From:** Holm Karin

**Sent:** 23 June 2014 16:05

**To:** 'Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com))'; 'Bachtar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id))'; 'Xavier.Kurz@ema.europa.eu';  
'Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu))'; 'David.Martin@fda.hhs.gov'; 'terhi.kilpi@thl.fi'; Bergman Ulf  
**Cc:** 'Jouquelet-Royer, Corinne'; 'Francoise.Sillan@sanofipasteur.com'; 'Darko, Mimi ((b)(6))'

**Subject:** RE: Doodle: Link for poll "CIOMS WG on VS TG2 section 5"

*Dear Dawei Liu, Novi, Xavier, Irina, David, Terhi, Ulf...*

*We haven't yet heard from you if you are available at these times and we are trying to find the best time for a TC to work on Section 5 of the Manual on Active Safety Surveillance....*

Hi, CIOMS WG on VS - TG2 Active Surveillance section 5

Corinne Jouquelet-Royer and Harry Seifert would like to have a TC to start the process moving on drafting section 5. Please let us know if you would be available any of these times by clicking on this doodle poll...



<http://doodle.com/b6z8aicfaia92fbt>

Thank you,  
Karin

Most popular date: Friday, June 27, 2014 12:00 PM |

Top of Form

	June 2014		July 2014
	Fri 27	Tue 1	Wed 2
7 participants	12:00 PM	5:00 PM	6:00 PM
Karin Holm		✓	
corinne jouquelet	✓	✓	✓
royer	✓		✓
Harry Seifert	✓	✓	✓
Patrick Zuber	✓		
Christine Maure	✓		
Scott Winiecki	✓		✓
Frank DeStefano			
	Friday, June 27, 2014 12:00 PM	Tuesday, July 1, 2014 5:00 PM	Wednesday, July 2, 2014 6:00 PM

Bottom of Form

\*\*\*\*\*

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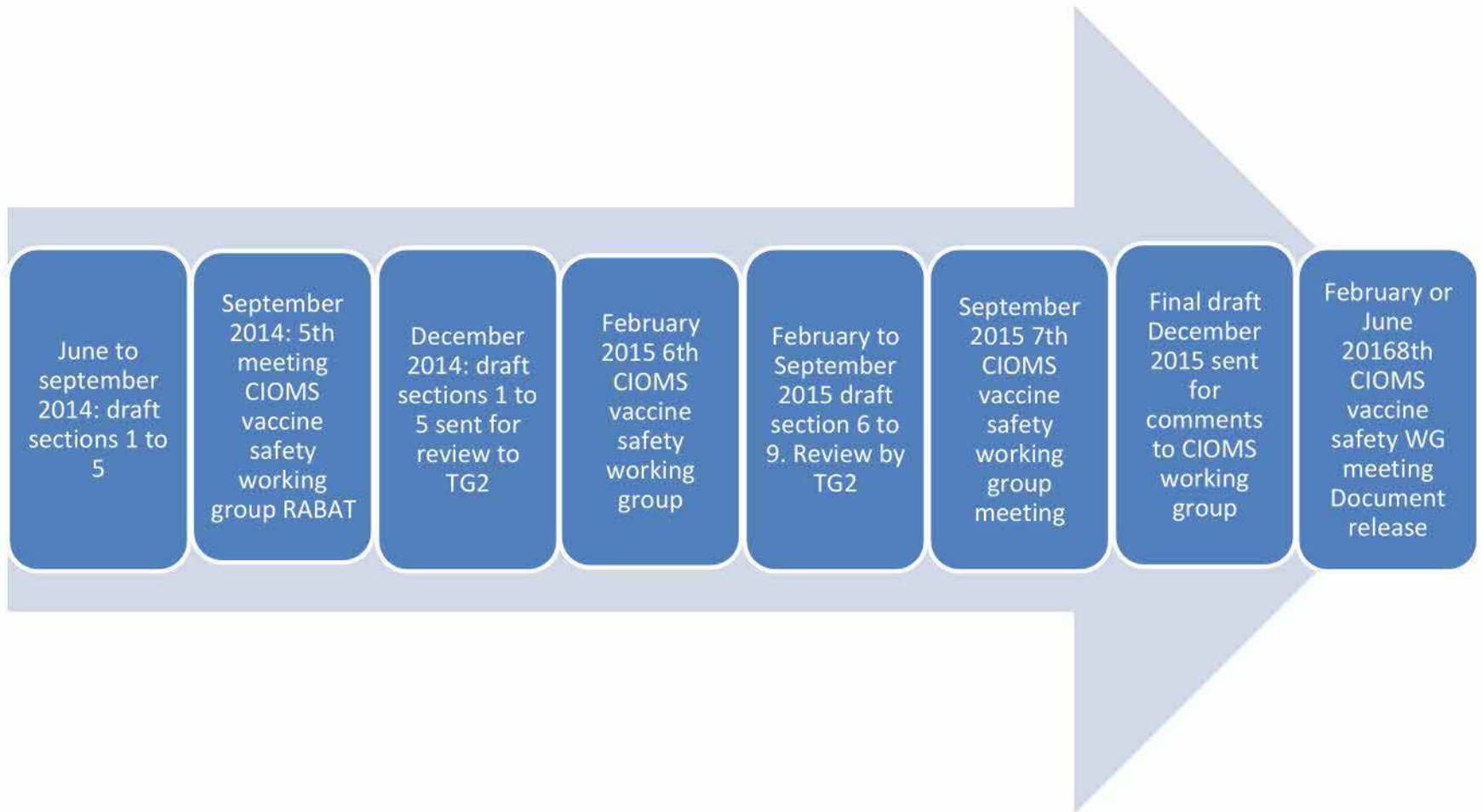
# CIOMS VACCINE SAFETY WORKING GROUP

TOPIC GROUP 2 Development of  
section 527 June 2014

# AGENDA

- Review of the section 5 to get alignment and shared understanding on what need to be achieved Agree on contributors to which sections. Agree on How we will work together? And timelines for draft and reviews before September meeting

# Key steps



# Actions from Last Meetings

- Idea to add examples of successful and unsuccessful active surveillance systems throughout the text (not just in section 10). Suggestion to add a literature search for additional examples. Some examples at GAVCS included studies conducted in northern Ghana and India. Although example are essential to illustrate the topics, it is critical to provide as well clear criteria to set up and conduct active surveillance systems. This is what has been done in preparation of malaria vaccine introduction. Choose also examples of not successful active surveillance. Something about MeninAfriVac seemed population-based but turned out to be case finding from sentinel sites (?) The links proposed to be provided (see section 3-Strategy of the Business plan) in the document should be accompanied by explanation. Think about the involvement of external experts at the time of the review of the draft document (additional funds needed).

# List of volunteers

- Leaders : Harry Seifert , Corinne Jouquelet-Royer  
Contributors Liu Dawei Novilia Bachtiar  
Xavier Kurtz & Irina Caplanusi David Martin and Scott Winieky  
Frank Destefano Tehri Kilpi

# Section 5 Overview

Section & Sub sections	Key Content	Contributors	Action Items
5.1 . Rationale for ASS (fomer a)	<ul style="list-style-type: none"> <li>Need to define the scope</li> </ul>	DavidXavier	<ul style="list-style-type: none"> <li>Reach out to section 4 leader End of July / Beginning Aug</li> </ul>
5.2. Points to consider for setting up a ASS (former c, b, d)	1. Who ? When?Where?	1. NoviliaWHO representative (TBC) and FrancoiseTBC ???	
5.3 How ( e) including examples	How?	Tehri	
5.4. Governance	Oversight of studyGovernance on decision making	Corinne WHO representative?	

# Next steps

- Literature search : propose key words and ask the library ( Sanofipasteur ) : W 28 Corinne to circulate updated slides to people who did not attend and ask for additional contributors Scope of ASS: will be shared by Xavier and David end July early August First draft to be sent to Harry and Co by Week 36 ( Sept 3) . Harry and Co to collate a doc for review TC for review of comments on Week 37

**From:** Corinne.Jouquelet-Royer@sanofipasteur.com  
**Sent:** Fri, 27 Jun 2014 09:43:05 +0000  
**To:** holmk@cioms.ch; Harry.A.Seifert@gsk.com; Zuber, Patrick (CDC who.int); maurec@who.int; Winiecki, Scott (FDA/CDER); terhi.kilpi@thl.fi; novilia@biofarma.co.id; Destefano, Frank (CDC/OID/NCEZID); liudw929@126.com; Xavier.Kurz@ema.europa.eu; Irina.Caplanusi@ema.europa.eu; Martin, David (FDA/CDER); bergmanu@cioms.ch; Steven.R.Bailey@pfizer.com; Ayman.Ayoub@pfizer.com  
**Cc:** Francoise.Sillan@sanofipasteur.com; mimidarko66@yahoo.co.uk; bergmanu@cioms.ch  
**Subject:** RE: CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon (French time)  
**Attachments:** TG2 TC Section 5 June 27.pptx

Dear all,

You will find attached the slides for our meeting today .

Sorry for the short notice

Regards

Corinne

**Corinne Jouquelet-Royer, MD**

Head Global Pharmacovigilance  
TEL.: +33 (0)4.37.66.97.47 - CELL.: +33 (0)6.32.04.99.97  
SIÈGE MONDIAL - 2, AVENUE PONT PASTEUR - 69367 LYON cedex 07 - France

Please consider the environment before printing this email!

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** mardi 24 juin 2014 17:36  
**To:** Jouquelet-Royer, Corinne (sanofi pasteur); 'Harry.A.Seifert@gsk.com'; 'Patrick Zuber (zuberp@who.int)'; 'maurec@who.int'; 'Winiecki, Scott'; 'terhi.kilpi@thl.fi'; 'Bachtar (novilia@biofarma.co.id)'; 'fxd1@cdc.gov'; 'Dawei, Liu (liudw929@126.com)'; 'Xavier.Kurz@ema.europa.eu'; 'Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu)'; 'David.Martin@fda.hhs.gov'; Bergman Ulf; 'Bailey (Steven.R.Bailey@pfizer.com)'; Ayman.Ayoub@pfizer.com  
**Cc:** Sillan, Francoise (sanofi pasteur); 'Darko, Mimi (mimidarko66@yahoo.co.uk)'; Bergman Ulf  
**Subject:** RE: CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon (French time)

Dear CIOMS TG2 section 5 Contributors:

Corinne and Harry are looking forward to talking with you on: **Fri 27 June 12noon (French time)**  
Attached please find the latest version of the business plan (including the Manual Table of Contents) for discussion.

**Agenda for TC**

- Quick review of the section 5 to get alignment and shared understanding on what need to be achieved
- Agree on contributors to which sections



- And timelines for draft and reviews before September meeting

#### Sanofi Telecon dial in numbers

France : (b)(6) (local)  
 Canada : (b)(6) (local)  
 US : (b)(6) (local)  
 Belgique : (b)(6) (local)  
 Singapore : (b)(6)  
 Mexique : (b)(6)

Participant code : 6505806850#

Code PIN (CP) : 1078#

Additional Numbers can be found here: <http://www.intercall.com/sanofi/numbers/index.htm>

Wishing you good connections and hope all try to speak clearly, loudly, slowly for optimal communication!

Karin

#### Karin R. Holm

Technical Coordinator, Working Group on Vaccine Safety  
 Publications Consultant, Working Group IX Risk Minimization  
 Council for International Organizations of Medical Sciences (CIOMS)  
 Associate partner of UNESCO / In official relations with WHO  
 c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
 Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
 Email: [holm@cioms.ch](mailto:holm@cioms.ch)

---

**From:** Holm Karin

**Sent:** 24 June 2014 11:36

**To:** Jouquelet-Royer, Corinne; [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); Patrick Zuber ([zuberp@who.int](mailto:zuberp@who.int)); [maurec@who.int](mailto:maurec@who.int); Winiecki, Scott; [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); Bachtiar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); [Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu); Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; Bailey ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com))  
**Cc:** [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); Darko, Mimi ([mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk))  
**Subject:** CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon (French time)

Dear CIOMS TG2 Chapter 5 Contributors,

Corinne Jouquelet-Royer (Sanofi, who is new to the CIOMS WG but will eventually take over at some point in the future for Françoise, who is moving to a new area at Sanofi) and Harry Seifert (GSK) kindly offered to organize Chapter 5 of the Manual on Active Safety Surveillance. Ch.5 is the “meat of the manual” on Establishing Active Surveillance (see Table of Contents in business plan draft attached).

The best day/time was this Friday, 27 June, 12pm French time. Sanofi kindly will arrange TC and send instructions on how to access.

#### Agenda for TC

- Quick review of the section 5 to get alignment and shared understanding on what need to be achieved
- Agree on contributors to which sections
- And timelines for draft and reviews before September meeting

	June 2014
	Fri 27
	12:00 PM
Karin Holm	NO
corinne jouquelet royer	OK
Harry Seifert	OK
Patrick Zuber	OK
Christine Maure	OK
Scott Winiecki (FDA)	OK
Frank DeStefano	NO
Terhi Kilpi	OK
Novilia Sjafri Bachtiar	OK
Xavier Kurz	OK
Dawei Liu	?
Irina Caplanusi	?
David Martin	?
Ayman Ayoub	?
Steven Bailey	NO
Ulf Bergman	NO
Count	8

**Karin R. Holm**

Technical Coordinator, Working Group on Vaccine Safety  
 Publications Consultant, Working Group IX Risk Minimization  
 Council for International Organizations of Medical Sciences (CIOMS)  
 Associate partner of UNESCO / In official relations with WHO  
 c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
 Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
 Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

---

**From:** Holm Karin

**Sent:** 23 June 2014 16:05

**To:** 'Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com))'; 'Bachtiar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id))'; 'Xavier.Kurz@ema.europa.eu';

'Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu))'; 'David.Martin@fda.hhs.gov'; 'terhi.kilpi@thl.fi'; Bergman Ulf

**Cc:** 'Jouquelet-Royer, Corinne'; 'Francoise.Sillan@sanofipasteur.com'; 'Darko, Mimi ([mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk))'

**Subject:** RE: Doodle: Link for poll "CIOMS WG on VS TG2 section 5"

*Dear Dawei Liu, Novi, Xavier, Irina, David, Terhi, Ulf...*

*We haven't yet heard from you if you are available at these times and we are trying to find the best time for a TC to work on Section 5 of the Manual on Active Safety Surveillance....*

Hi, CIOMS WG on VS - TG2 Active Surveillance section 5

Corinne Jouquelet-Royer and Harry Seifert would like to have a TC to start the process moving on drafting section 5. Please let us know if you would be available any of these times by clicking on this doodle poll...

<http://doodle.com/b6z8aicfaia92fbt>

Thank you,  
Karin

Most popular date: Friday, June 27, 2014 12:00 PM |

Top of Form

	June 2014		July 2014
	Fri 27	Tue 1	Wed 2
7 participants	12:00 PM	5:00 PM	6:00 PM
Karin Holm		✓	
corinne jouquelet	✓	✓	✓
royer			
Harry Seifert	✓	✓	✓
Patrick Zuber	✓		
Christine Maure	✓		
Scott Winiecki	✓		✓
Frank DeStefano			
	Friday, June 27, 2014	Tuesday, July 1, 2014	Wednesday, July 2, 2014
	12:00 PM	5:00 PM	6:00 PM

Bottom of Form

\*\*\*\*\*  
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# CIOMS VACCINE SAFETY WORKING GROUP

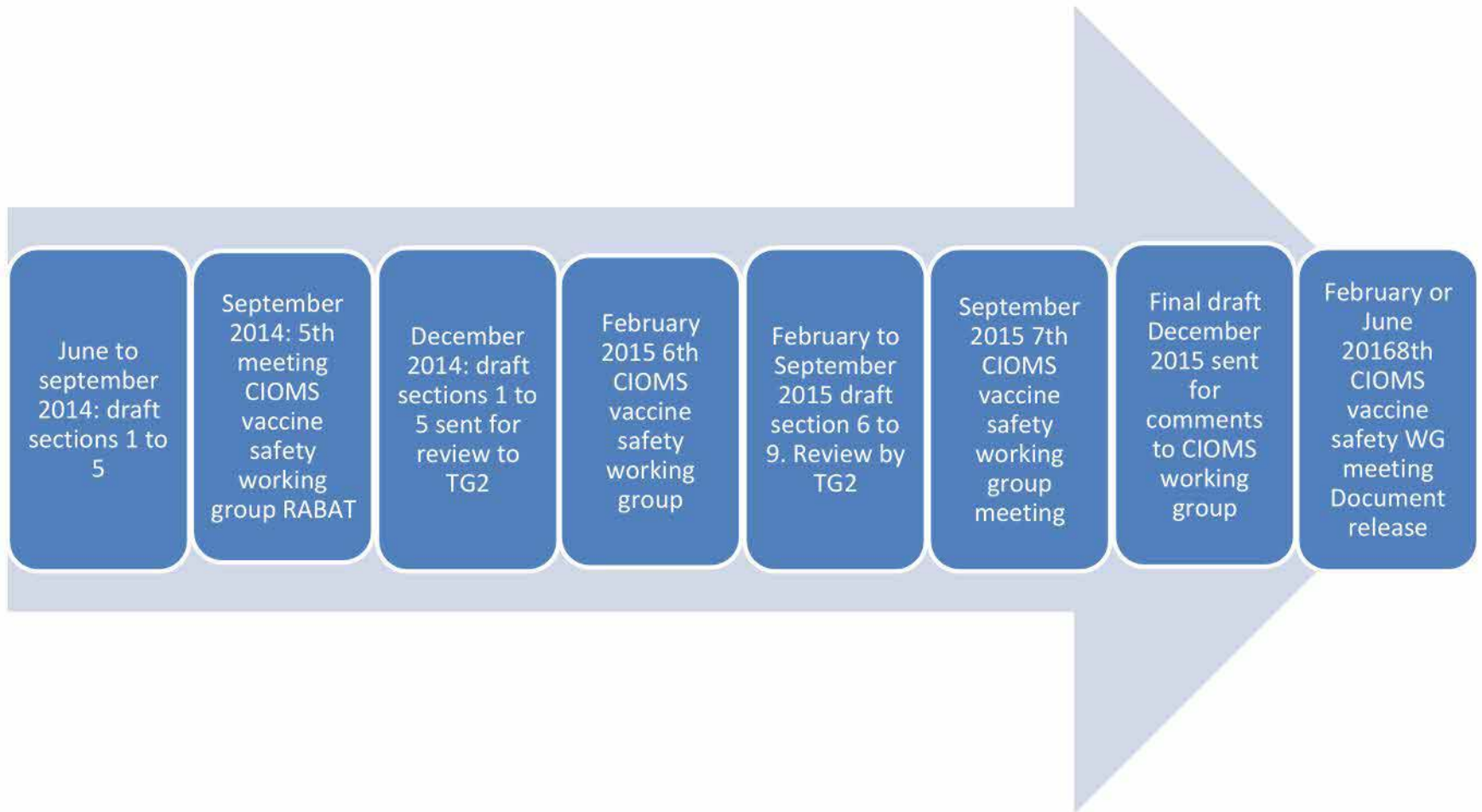
TOPIC GROUP 2 Development of  
section 5

# AGENDA

- Review of the section 5 to get alignment and shared understanding on what need to be achieved Agree on contributors to which sections. Agree on How we will work together? And timelines for draft and reviews before September meeting



# Key steps



# Actions from Last Meetings

- Idea to add examples of successful and unsuccessful active surveillance systems throughout the text (not just in section 10). Suggestion to add a literature search for additional examples. Some examples at GAVCS included studies conducted in northern Ghana and India. Although example are essential to illustrate the topics, it is critical to provide as well clear criteria to set up and conduct active surveillance systems. This is what has been done in preparation of malaria vaccine introduction. Choose also examples of not successful active surveillance. Something about MeninAfriVac seemed population-based but turned out to be case finding from sentinel sites (?) The links proposed to be provided (see section 3-Strategy of the Business plan) in the document should be accompanied by explanation. Think about the involvement of external experts at the time of the review of the draft document (additional funds needed).

# List of volunteers

- Leaders : Harry Seifert , Corinne Jouquelet-Royer  
Contributors Liu Dawei Novilia Bachtiar  
Xavier Kurtz & Irina Caplanusi David Martin and Scott Winieky  
Frank Destefano Tehri Kilpi



# Section 5 Overview

Section & Sub sections	Contributors	Key Content	Action Items
5.1 Rationale for ASS (a)			
5.2 Points to consider for setting up (c, b, d)			
5.3 How ( e) including examples ( ?)			
5.4 Governance			

# Section 5.1 Overview

# Lead : ?

[illegible]

## Section 5.2 Overview

# Lead: ?

[illegible]

## Section 5.3 Overview

# Lead: ?

[illegible]

## Section 5.4 Overview

# Lead: ?

[illegible]

# Next steps

**From:** Francoise.Sillan@sanofipasteur.com  
**Sent:** Thu, 19 Jun 2014 09:58:35 +0000  
**To:** holmk@cioms.ch;maurec@who.int;Corinne.Jouquelet-Royer@sanofipasteur.com;Zuber, Patrick (CDC who.int);bergmanu@cioms.ch;atebaa@yahoo.fr;Steven.R.Bailey@pfizer.com;Ayman.Ayoub@pfizer.com;Destefano, Frank (CDC/OID/NCEZID);novilia@biofarma.co.id;Harry.A.Seifert@gsk.com;Patricia.Mandali@anvisa.gov.br;ulrich.heininger@ukbb.ch;dongduo@cdr.gov.cn;Martin, David (FDA/CDER);KHGo@AIM.EDU;Dirk.Mentzer@pei.de;Doris.Oberle@pei.de;terhi.kilpi@thl.fi;Irina.Caplanusi@ema.europa.eu;Xavier.Kurz@ema.europa.eu  
**Cc:** jiguate@who.int  
**Subject:** RE: CIOMS TG2 Active Surv - Thursday, 19 June, 3pm  
**Attachments:** TG2 TC June 19.pptx

Dear all

Please find enclosed the agenda for today's meeting and key elements of the business plan to guide our discussion

Thank you for your participation and talk to you soon!

*Best regards / Bien cordialement,*

*Françoise*

---

**De :** Holm Karin [mailto:holmk@cioms.ch]

**Envoyé :** lundi 16 juin 2014 15:36

**À :** 'MAURE, Christine'; Sillan, Francoise (sanofi pasteur); Jouquelet-Royer, Corinne (sanofi pasteur); Patrick Zuber (zuberp@who.int); Bergman Ulf; atebaa@yahoo.fr ; Bailey (Steven.R.Bailey@pfizer.com); Ayman.Ayoub@pfizer.com; fxd1@cdc.gov; Bachtiar (novilia@biofarma.co.id); Harry.A.Seifert@gsk.com; Patricia.Mandali@anvisa.gov.br; ulrich.heininger@ukbb.ch; dongduo@cdr.gov.cn; David.Martin@fda.hhs.gov; KHGo@AIM.EDU; Holm Karin; Dirk Mentzer; Oberle, Doris (alt2); 'Terhi Kilpi'; Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu); Xavier.Kurz@ema.europa.eu

**Cc :** JIGUET, Evelyn M. (jiguate@who.int)

**Objet :** CIOMS TG2 Active Surv - Thursday, 19 June, 3pm

Dear CIOMS TG2 Participants,

Please find the instructions below on how to join the teleconference call on THURSDAY, 19 JUNE, 3PM. (Thank you to WHO for arranging!)

Attached is the Arkadin list of toll-free or local numbers to call. NOTE! For participants from countries not listed in the attachment, they need to provide [jiguate@who.int](mailto:jiguate@who.int) with the phone number at least 48 hours prior the call, and they will be connected through ARKADIN.

Attached also is the draft of the business plan for TG2 to discuss on the TC.

Thank you for your participation!

Karin

**DIAL IN DETAILS:**





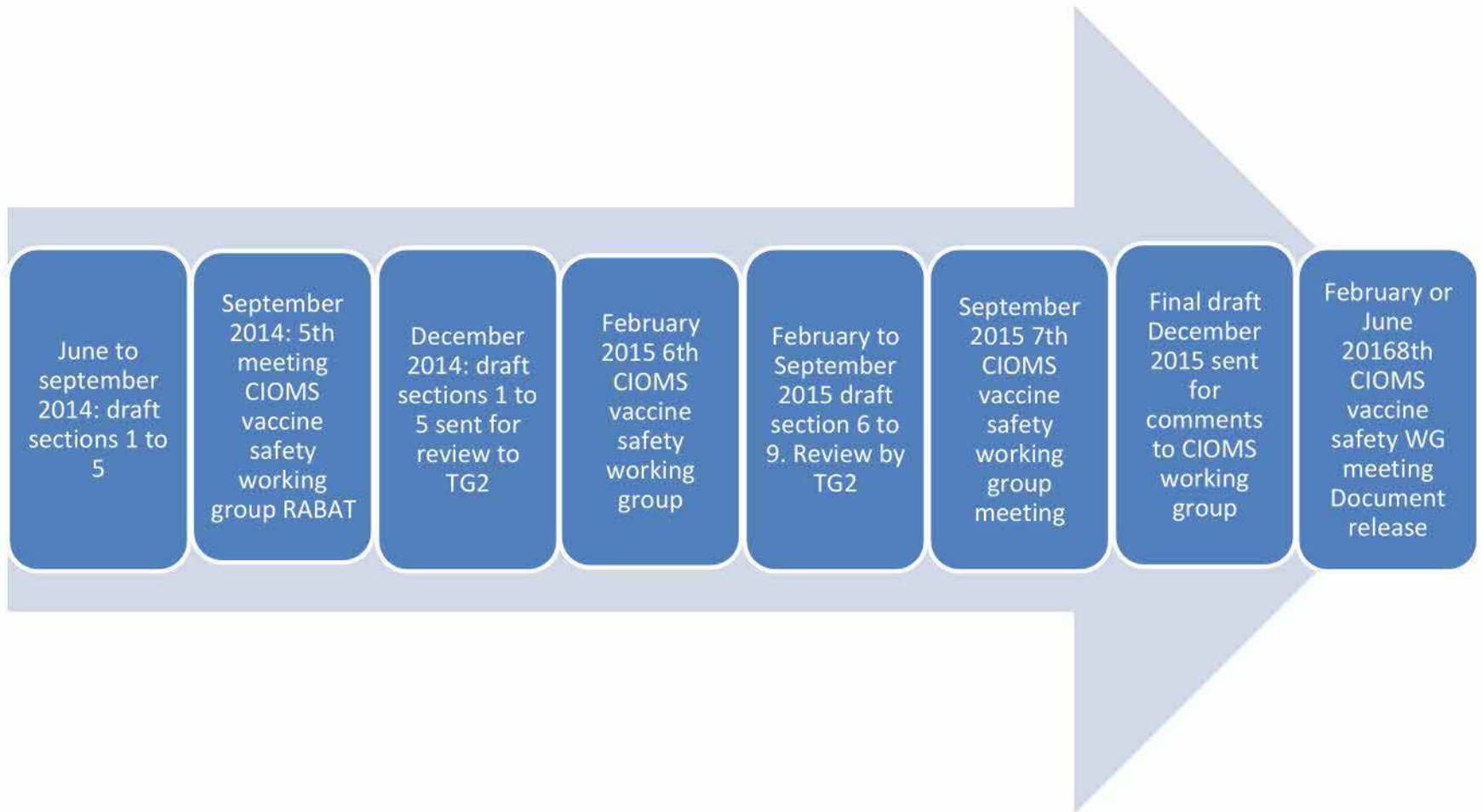
# CIOMS VACCINE SAFETY WORKING GROUP

TOPIC GROUP 2 Improvement of post  
marketing surveillance when launching  
a new vaccine in a LMIC

# AGENDA

- Comments on draft business plan  
Review of key steps  
Define leaders and contributors for sections 1 to 5

# Key steps



# Key contributors

## sections 1 to 5

Section	Leader	Contributors
<b>1-Glossary</b>		
<b>2-Abbreviations</b>		
<b>3-Purpose</b>		
<b>4-Post Marketing safety surveillance</b>		
<b>5-Establishing active safety surveillance</b>		

**From:** Kuter, Barbara J.  
**Sent:** Fri, 28 Mar 2014 16:34:51 -0400  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Wharton, Melinda (CDC/OID/NCIRD)  
**Subject:** RE: HPV Vaccine - Japan

Frank,

Thanks for all your work in the last 24 hours! I think the information you have provided thus far is sufficient. Let's see if a formal request comes from Japan. Then a comparison to background rates might be needed.

Have a great weekend!

Barb

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

From: Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxdl@cdc.gov>]  
Sent: Friday, March 28, 2014 4:16 PM  
To: Kuter, Barbara J.  
Cc: Wharton, Melinda (CDC/OID/NCIRD)  
Subject: RE: HPV Vaccine - Japan

Barb,

The age range of the 41 cases is 12 to 27 years (median 16). A comparison of VAERS reporting rates for fibromyalgia would require a lot of caveats, but it could be done. I am not sure what the background rate is for fibromyalgia or if there is even a reliable estimate. If you would like to discuss further, I could put you in contact with the medical officer in our office that deals with HPV vaccine, but she is out of the office until next week.  
Frank

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

From: Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
Sent: Friday, March 28, 2014 3:50 PM  
To: Destefano, Frank (CDC/OID/NCEZID)  
Cc: Wharton, Melinda (CDC/OID/NCIRD)  
Subject: RE: HPV Vaccine - Japan

Frank,

Thanks for these numbers - this is very helpful. Would it be appropriate to compare the reporting rate of fibromyalgia in VAERS (based on doses distributed) to a background rate of fibromyalgia in this age group (with the appropriate caveats)? If so, what background rate would you use, please?

And by any chance do you know the age range for the 41 cases reported?

Thanks again,

Barb

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

From: Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxdl@cdc.gov>]  
Sent: Friday, March 28, 2014 12:57 PM  
To: Kuter, Barbara J.  
Cc: Wharton, Melinda (CDC/OID/NCIRD)

Subject: RE: HPV Vaccine - Japan

The HPV/Fibromyalgia search includes all reports in VAERS from the time HPV4 vaccine was originally licensed (6/8/06) to reports received and processed (some reports received may not have been processed/entered yet) as of 3/27/14.

From the time of HPV4 vaccine licensure on 6/8/06 to 3/27/14, VAERS has received and processed a total of 27,300 US primary reports for HPV2, HPV4 or HPV<sub>x</sub>(HPV brand unknown) when given alone or in combination with other vaccines; 1971 (7.2%) were serious reports and 25,329 (92.78%) were non serious. A serious report is one in which at least one of the following was reported: death, life threatening illness, hospitalization, prolongation of an existing hospitalization or permanent disability.

From 6/8/06 to 3/27/14, VAERS has received and processed a total of 219,447 US primary reports after ALL vaccines. Of those 10,659 (4.86%) were serious and 208,788 (95.14%) were non serious.

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

From: Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
Sent: Friday, March 28, 2014 12:05 PM  
To: Destefano, Frank (CDC/OID/NCEZID)  
Cc: Wharton, Melinda (CDC/OID/NCIRD)  
Subject: RE: HPV Vaccine - Japan

Thanks, Frank, for the rapid response. I assume this search covered the period from 2006 to date. Can you please remind me of the total number of VAERS reports received over that period?

Barb

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

From: Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
Sent: Friday, March 28, 2014 9:59 AM  
To: Kuter, Barbara J.  
Cc: Wharton, Melinda (CDC/OID/NCIRD)  
Subject: RE: HPV Vaccine - Japan

Barb,

We searched VAERS for US primary reports coded as "FIBROMYALGIA" after HPV2, HPV4 or HPV<sub>x</sub>(HPV brand unknown) when given alone or in combination with other vaccines. VAERS contains 41 reports. Of those, 33 were for cases in which HPV4 was the only vaccine administered. Of the 41 reports, 25 were serious. Among the 25 serious reports, 5 were reported as a life threatening illness, 12 required hospitalization and 8 resulted in permanent disability.

I hope this helps,  
Frank

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

From: Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
Sent: Thursday, March 27, 2014 2:40 PM  
To: Destefano, Frank (CDC/OID/NCEZID)  
Cc: Wharton, Melinda (CDC/OID/NCIRD)  
Subject: RE: HPV Vaccine - Japan

Frank,

Thanks for your rapid response. If you could take a quick look at this in VAERS, that would be helpful. Of course, we recognize the limitations of doing so.



Thanks again,

Barb

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

From: Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxdl@cdc.gov>]

Sent: Thursday, March 27, 2014 1:51 PM

To: Kuter, Barbara J.; Wharton, Melinda (CDC/OID/NCIRD)

Subject: RE: HPV Vaccine - Japan

Barb,

We have not been contacted about this. We also are not aware of any literature or other data on HPV vaccine and CTD's. We have not looked at fibromyalgia in VSD or VAERS. This is a complex diagnosis and does not lend itself to a quick analysis in either system, but for what it would be worth (which may be little) we could take a look at reports submitted to VAERS.

Thanks for bringing this to our attention, Frank

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

From: Kuter, Barbara J. [[mailto:barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]

Sent: Thursday, March 27, 2014 11:38 AM

To: Wharton, Melinda (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID)

Subject: HPV Vaccine - Japan

Melinda and Frank,

We just received the attached English translation of a news item from Japan describing a preliminary study of patients with connective tissue disorder (rheumatoid arthritis and fibromyalgia) and their use of HPV vaccines. The information is based on a presentation made at a health seminar by a local investigator from the Japanese College of Fibromyalgia (JCFI), Tokyo Medical University. The JCFI has asked MHLW to conduct further research in this area.

We will be looking at our own pre & postlicensure safety data to address this question, but thought it would be helpful to find out if CDC has also been contacted to provide any data. Can you please tell me if you have looked at fibromyalgia in either VAERS or VSD or might be able to do so? We have not found any evaluation of this particular AE in the literature.

Any information you can share with us would be much appreciated.

Thanks.

Barb

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**From:** Kuter, Barbara J.  
**Sent:** Thu, 27 Mar 2014 11:37:43 -0400  
**To:** Wharton, Melinda (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** HPV Vaccine - Japan  
**Attachments:** 20140326 Eng MTPPro.docx

Melinda and Frank,

We just received the attached English translation of a news item from Japan describing a preliminary study of patients with connective tissue disorder (rheumatoid arthritis and fibromyalgia) and their use of HPV vaccines. The information is based on a presentation made at a health seminar by a local investigator from the Japanese College of Fibromyalgia (JCFI), Tokyo Medical University. The JCFI has asked MHLW to conduct further research in this area.

We will be looking at our own pre & postlicensure safety data to address this question, but thought it would be helpful to find out if CDC has also been contacted to provide any data. Can you please tell me if you have looked at fibromyalgia in either VAERS or VSD or might be able to do so? We have not found any evaluation of this particular AE in the literature.

Any information you can share with us would be much appreciated.

Thanks.

Barb

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Translation: MT Pro March 26, 2014

## **Pain after HPV vaccination caused by immune abnormalities in the brain – ASIA syndrome?**

**Japan College of Fibromyalgia Investigation conducts preliminary study**



There are occasional reports of generalized pain similar to fibromyalgia mainly among junior and senior high school students in association with human papillomavirus (HPV) vaccination designed to prevent cervical cancer. At a health seminar held in Tokyo by the Japan Medical Research Foundation on March 23, Kusuki Nishioka, president of the Japan College of Fibromyalgia Investigation (JCFI) and director of Institute of Medical Science, Tokyo Medical University, said that the results of a preliminary study conducted by the JCFI indicate that the pain may be Autoimmune Syndrome induced by Adjuvants (ASIA), immune disorders in the brain induced by adjuvants that increase immune response after the vaccination. The JCFI announced that it will perform a full-scale study of HPV vaccine recipients.

**Study finds immune disorder of anti-NMDA receptor antibodies**



西岡 久寿樹 氏

Nishioka and the JCFl conducted a preliminary study of 96 patients with connective tissue diseases (89 females) including 12 cases of rheumatoid arthritis and 74 cases of fibromyalgia at three of 138 institutions in the JCFl network. Conducted between February 20 and March 20, the survey studied whether subjects have received the vaccination and whether they have adverse reactions. The results show that 55 among 96 patients have received HPV vaccination and 8 patients have suffered from unexplained generalized pain or severe arthritis after vaccination. Most of them were teenagers. While many of these patients sought medical attention suspecting fibromyalgia, pregabalin for the treatment of neuropathic pain was not effective in most cases.

One patient had positive tender points relating to juvenile fibromyalgia while no good result was attained with environmental isolate, which is considered effective. No abnormality was found in blood tests. Because the patient had auditory and visual hallucination, illusion, and personality disorder, physicians suspected acute encephalopathy. A detailed examination found significant increase in anti-N-methyl-D-aspartate receptor antibodies. The patient was diagnosed as having anti-NMDA receptor encephalitis under Shunpei Yokota, professor of pediatrics, Yokohama City University. The patient underwent steroid pulse therapy, which showed certain effect.

Nishioka further pointed out the possibility of ASIA, which shows symptoms such as severe muscle pain, arthritis, cognitive impairment, and sleeping disorder accompanied by neurological symptoms. The HPV vaccines contain aluminum and other materials as adjuvants to boost immune response. These new types of adjuvants may pass through blood-brain barrier using macrophage and cause autoimmune disorders in the brain.

At the end, Nishioka said that the JCFI had requested the Minister of Health, Labor and Welfare to conduct a survey after April to collect objective data on delayed adverse reactions that appear several months to several years after HPV vaccination as well as causal relationship with chronic pain and other symptoms.

According to Nishioka, Director-General of MHLW's Health Service Bureau visited him on March 24 to discuss various topics. He said that adverse reactions of the vaccination are not caused by mental factors and that it would be adequate to fully discontinue vaccination if any problem is found after serious investigations by the MHLW and relevant academic groups because there are quite a few reports of serious adverse reactions and there are many people who are suspicious about the benefit of the vaccination. Nishioka said that Director-General of Health Service Bureau indicated the intention to make reviews without delay.



**From:** Francoise.Sillan@sanofipasteur.com  
**Sent:** Mon, 20 Jan 2014 10:41:31 +0000  
**To:** holmk@cioms.ch; alexooo@yahoo.com; alex.dodoo@umcafrica.org; owdena@cioms.ch; atebaa@yahoo.fr; Ayman.Ayoub@pfizer.com; William.Gregory@pfizer.com; Brigitte.Keller-Stanislawski@pei.de; maurec@who.int; Vellozzi, Claudia (CDC/OID/NCHHSTP); Martin, David (FDA/CDER); liudw929@126.com; Dirk.Mentzer@pei.de; Destefano, Frank (CDC/OID/NCEZID); sjolinforsbergg@cioms.ch; Harry.A.Seifert@gsk.com; j.bonhoeffer@brightoncollaboration.org; KHGo@AIM.EDU; mceuppe1@its.jnj.com; Marie.Lindquist@who-umc.org; PatelMayur@MedImmune.com; BlumM@medimmune.com; mimidarko66@yahoo.co.uk; reg\_airs\_egyvac@hotmail.com; novilia@biofarma.co.id; Patricia.Mandali@anvisa.gov.br; Zuber, Patrick (CDC who.int); Paulo.santos@bio.fiocruz.br; Peter.Arlett@ema.europa.eu; drpsk@seruminstitute.com; raja.benkirane@gmail.com; rroten@its.jnj.com; Rmenezes@bio.fiocruz.br; sidarta.silva@anvisa.gov.br; sten.olsson@who-umc.org; Steven.R.Bailey@pfizer.com; terhi.kilpi@thl.fi; ulrich.heininger@ukbb.ch; Xavier.Kurz@ema.europa.eu  
**Cc:** Sabine.Garnier@sanofipasteur.com  
**Subject:** RE: CIOMS vaccine safety TG2 surveillance TC 20Jan 2 to 4pm (French time)

Dear all

Please find enclosed the web link to the intercall service for more instructions.

If you don't find instructions for your country, you can call the phone number of the nearest country or let me know if there is a phone number where we can call you

<http://www.intercall.com/sanofi/numbers/index.htm>

I copy our assistant, Sabine, who will help me in the organization.

Talk to you soon,

*Best regards / Bien cordialement,*

*Françoise*

---

**De :** Holm Karin [mailto:holmk@cioms.ch]

**Envoyé :** lundi 20 janvier 2014 11:19

**À :** 'Alex Dodoo'; 'Alex Dodoo UMC'; Owden Amanda; 'Amina Tebaa'; Ayman.Ayoub@pfizer.com; 'Bill Gregory'; 'Brigitte Keller-Stanislawski'; 'Christine Maure (alt)'; 'Claudia Vellozzi'; 'David Martin'; 'Dawei, Liu'; Dirk Mentzer; Sillan, Francoise (sanofi pasteur); 'Frank DeStefano (alt)'; Sjolín Forsberg Gunilla; 'Harry Seifert (alt)'; Holm Karin; 'Jan Bonhoeffer (alt)'; 'Kenneth Y. Hartigan-Go'; 'Marc Ceuppens'; 'Marie Lindquist'; 'Mayur Patel (alt)'; 'Michael Blum'; 'Mimi Darko Delese (alt)'; 'Mona Hassan Abu Youssef'; 'Novilia Sjafrí Bachtiar'; 'Patricia Mandali de Figueiredo'; 'Patrick Zuber'; 'Paulo Gomes dos Santos (alt)'; 'Peter Arlett (alt)'; 'Prasad Kulkarni'; 'Raja Benkirane (alt)'; 'Raphaelé Roten'; 'Reinaldo de Menezes Martins'; Silva Sidarta (sidarta.silva@anvisa.gov.br); 'Sten Olsson (alt)'; 'Steven Bailey'; 'Terhi Kilpi'; 'Ulrich Heininger'; 'Xavier Kurz'

**Objet :** CIOMS vaccine safety TG2 surveillance TC 20Jan 2 to 4pm (French time)

Dear WG members,

If you are interested in participating in the TC for Topic Group2 Surveillance Strategy, you are most welcome. Attached find the free or local call numbers. The participant's code will be:

6728829242#. Thank you to Sanofi-Pasteur for sponsoring the TC.

Karin

The TC for Topic Group 2 will be on January 20 from 2 to 4 pm (French time); I send you enclosed the call numbers, the participant's code will be: 6728829242#. Let me know the final list of participants and I will send the invitation.

Thank you,

*Best regards / Bien cordialement,*

Françoise

## Topic Group 2: Surveillance Strategy

Leads: Françoise Sillan & Mimi Darko Delese

TC: Monday, January 20, 2:00pm Central European Time

Including: Amina Tebaa, Mona Youssef, Patrick Zuber, Harry Siefert, Christine Maure (alt), Novilia Bachtiar, Claudia Vellozzi, Alex Dodoo, Frank DeStefano (alt), Steven Bailey (alt), Bill Gregory, Harry Siefert (alt), David Martin, Michael Nguyen (alt)

Reps: Moroccan Centre PhV, EgyptVac, WHO, GSKBio, PT Bio Farma Indonesia, CDC, Ghana FDA, US FDA, GSKBio, Pfizer

Possible topics to discuss...

- Spontaneous reporting system improvements and post-marketing surveillance study: necessity to implement for new vaccines.
- Identification of new products and subsequent vaccine safety issues that will be generated when certain products are distributed for the first time in LMICs: a.) Spontaneous reporting system improvements, b.) Cohort Event Monitoring.
- CIOMS WG should define minimum capacity for post marketing surveillance.

\*\*\*\*\*  
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\*\*\*\*\*

**From:** Cristina Masseria  
**Sent:** Wed, 20 Nov 2013 18:54:40 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein;Shanthy Krishnarajah  
**Subject:** (b)(4)

Dear Dr De Stefano,

(b)(4)

Please let us know your availability.

Thank you very much.  
Best regards,  
Cristina

*Cristina Masseria, PhD  
GlaxoSmithKline  
US Health Outcomes and Medical Policy - Vaccines  
Phone: +1.215.751.4960*

**From:** Harry Seifert  
**Sent:** Tue, 5 May 2015 13:49:19 +0000  
**To:** McNeil, Michael (CDC/OID/NCEZID)  
**Cc:** Destefano, Frank (CDC/OID/NCEZID); Brown, Harriet (CDC/OID/NCEZID); Jackson, Charla (CDC/ONDIEH/NCIPC); Roberts, Traci Sinetta (CDC/OID/NCEZID); Brown, Harriet (CDC/OID/NCEZID); Greg Powell  
**Subject:** GSK presentation for May 7th ISO Hot Topics meeting

Dear Mike,

Attached is our PowerPoint presentation for Thursday's Hot Topics session. You are welcome to share these internally, but please regard the contents as proprietary and don't distribute them beyond the CDC.

I have included a conflict of interest slide. Our conflict of interest should be self-evident, but I ask that you please keep it in the presentation so there is no question about our transparency.

Looking forward to meeting with you and the team and hearing your thoughts.

Best regards,

Harry Seifert  
Cell 610-716-3077



**From:** Whary, Maryellen  
**Sent:** Tue, 14 May 2013 14:03:58 -0400  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: Teleconf. w/Frank DeStefano from the CDC re presentation at June ACIP on rotavirus vaccines and intussusception

Please forward call details. Thank you.

Maryellen Whary (works Monday, Tuesday, Wednesday)  
Robyn Mowrer (works Thursday, Friday)  
WP97-A345 - phone: 215-652-9445/fax: 215-993-1848  
maryellen\_whary@merck.com/robyn\_mowrer@merck.com

-----Original Appointment-----

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Tuesday, May 14, 2013 2:02 PM  
**To:** Whary, Maryellen  
**Subject:** Accepted: Teleconf. w/Frank DeStefano from the CDC re presentation at June ACIP on rotavirus vaccines and intussusception  
**When:** Friday, May 31, 2013 10:30 AM-11:30 AM (UTC-05:00) Eastern Time (US & Canada).  
**Where:** Frank to provide teleconf. info.--will forward once I receive

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**From:** Kuter, Barbara J.  
**Sent:** Thu, 5 Nov 2015 11:47:42 -0500  
**To:** Markowitz, Lauri (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); Wharton, Melinda (CDC/OID/NCIRD)  
**Subject:** HPV referral (EMA Article 20) - Final Report on CRPS & POTS  
**Attachments:** HPV - PRAC Final Report - CRPS & POTS - Nov 5, 2015.pdf

The PRAC has just issued a press release & final summary of the Article 20 referral related to CRPS & POTS and HPV vaccines.

The title of the summary report says "Review concludes evidence does not support that HPV vaccines cause CRPS or POTS.

Reports of CRPS and POTS after HPV vaccination are consistent with what would be expected in this age group."

Here is the link to the press release & a PDF of the actual report. Both can be found on the EMA/PRAC website.

<http://www.ema.europa.eu/ema/index.jsp?>

Barb

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EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

5 November 2015  
EMA/714950/2015

## Review concludes evidence does not support that HPV vaccines cause CRPS or POTS

Reports of CRPS and POTS after HPV vaccination are consistent with what would be expected in this age group

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has completed a detailed scientific review of the evidence surrounding reports of two syndromes, complex regional pain syndrome (CRPS) and postural orthostatic tachycardia syndrome (POTS) in young women given human papillomavirus (HPV) vaccines. These vaccines are given to protect them from cervical cancer and other HPV-related cancers and pre-cancerous conditions. This review concluded that the evidence does not support a causal link between the vaccines (Cervarix, Gardasil/Silgard and Gardasil-9) and development of CRPS or POTS. Therefore there is no reason to change the way the vaccines are used or amend the current product information.

CRPS is a chronic pain syndrome affecting a limb, while POTS is a condition where the heart rate increases abnormally on sitting or standing up, together with symptoms such as dizziness, fainting and weakness, as well as headache, aches and pains, nausea and fatigue. In some patients they can severely affect the quality of life. The syndromes are recognised to occur in the general population, including adolescents, regardless of vaccination.

PRAC thoroughly reviewed the published research, data from clinical trials and reports of suspected side effects from patients and healthcare professionals, as well as data supplied by Member States. It also consulted a group of leading experts in the field, and took into account detailed information received from a number of patient groups that also highlighted the impact these syndromes can have on patients and families.

Symptoms of CRPS and POTS may overlap with other conditions, making diagnosis difficult in both the general population and vaccinated individuals. However, available estimates suggest that in the general population around 150 girls and young women per million aged 10 to 19 years may develop CRPS each year, and at least 150 girls and young women per million may develop POTS each year. The review found no evidence that the overall rates of these syndromes in vaccinated girls were different from expected rates in these age groups, even taking into account possible underreporting. The PRAC noted that some symptoms of CRPS and POTS may overlap with chronic fatigue syndrome (CFS, also known as myalgic encephalomyelitis or ME). Many of the reports considered in the review have features of CFS and some patients had diagnoses of both POTS and CFS. Results of a large published study that showed no link between HPV vaccine and CFS were therefore particularly relevant.





The PRAC concluded that the available evidence does not support that CRPS and POTS are caused by HPV vaccines. Therefore there is no reason to change the way the vaccines are used or amend the current product information.

The review recognised that more than 80 million girls and women worldwide have now received these vaccines, and in some European countries they have been given to 90% of the age group recommended for vaccination. Use of these vaccines is expected to prevent many cases of cervical cancer (cancer of the neck of the womb, which is responsible for tens of thousands of deaths in Europe each year) and various other cancers and conditions caused by HPV. The benefits of HPV vaccines therefore continue to outweigh their risks. The safety of these vaccines, as with all medicines, will continue to be carefully monitored.

The PRAC's recommendations will now be passed to the Committee for Medicinal Products for Human Use (CHMP) for adoption of the Agency's final position. The evidence supporting the PRAC review will be published in an assessment report following the CHMP opinion.

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### **More about the medicine**

HPV vaccines are available in the European Union under the names Gardasil/Silgard, Gardasil 9, and Cervarix. Gardasil has been authorised since September 2006, and is approved for use in males and females for preventing precancerous growths and cancer in the cervix and anus, and genital warts. It protects against 4 types of HPV (types 6, 11, 16 and 18). Gardasil 9 (approved in June 2015) is used similarly but protects against 9 types of the virus (types 6, 11, 16, 18, 31, 33, 45, 52 and 58). Cervarix has been approved since September 2007 for use in women and girls to protect against precancerous growths and cancer in the cervix and genital area. It is active against types 16 and 18 of the virus. Following their approval, the vaccines have been introduced in national immunisation programs in many countries. It is estimated that more than 63 million girls and women worldwide have been vaccinated with Gardasil/Silgard and more than 19 million with Cervarix.

### **More about the procedure**

The review of HPV vaccines was initiated on 9 July 2015 by the European Commission at the request of Denmark, under Article 20 of Regulation (EC) No 726/2004.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. These PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's final opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.

---

### **Contact our press officer**

Monika Benstetter

Tel. +44 (0)20 3660 8427

E-mail: [press@ema.europa.eu](mailto:press@ema.europa.eu)

**From:** Kuter, Barbara J.  
**Sent:** Tue, 14 Jul 2015 18:27:34 -0400  
**To:** Markowitz, Lauri (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: Article 20 - EMA - HPV Vaccines - CONFIDENTIAL  
**Attachments:** WC500189476.pdf0.pdf, WC500189477.pdf0.pdf, WC500189478.pdf0.pdf, WC500189479.pdf0.pdf

Lauri & Frank,

Here are all the documents that were posted on the EMA website in regards to this review.

Please let me know if you have any questions.

Thanks.

Barb

---

**From:** Kuter, Barbara J.  
**Sent:** Friday, July 10, 2015 3:35 PM  
**To:** Markowitz, Lauri (CDC/OID/NCHHSTP); Destefano, Frank (CDC/OID/NCEZID) (fxd1@cdc.gov)  
**Subject:** Article 20 - EMA - HPV Vaccines - CONFIDENTIAL

Lauri & Frank,

Just a heads up. We were just informed that the Pharmacovigilance Risk Assessment Committee (PRAC) of the EMA will start a review of HPV vaccines to further clarify aspects of their safety profile. Specifically, the review will focus on rare reports of CRPS and POTS. The review does not question that the benefits of HPV vaccines outweigh their risks.

The official announcement from the EMA will be published online on Monday. I will send you a copy once available.

You may want to share with your colleagues as you may get questions or be asked for data.

Barb

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EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

13 July 2015  
EMA/454979/2015

## EMA to further clarify safety profile of human papillomavirus (HPV) vaccines

The European Medicines Agency (EMA) has started a review of HPV vaccines to further clarify aspects of their safety profile. These vaccines have been used in around 72 million people worldwide and their use is expected to prevent many cases of cervical cancer (cancer of the neck of the womb) and various other cancers and conditions caused by HPV. Cervical cancer is the 4<sup>th</sup> most common cause of cancer death in women worldwide, with tens of thousands of deaths in Europe each year despite the existence of screening programmes to identify the cancer early. The review does not question that the benefits of HPV vaccines outweigh their risks.

As for all licensed medicines the safety of these vaccines is monitored by the Agency's Pharmacovigilance Risk Assessment Committee (PRAC). The current review will look at available data with a focus on rare reports of two conditions: complex regional pain syndrome (CRPS, a chronic pain condition affecting the limbs) and postural orthostatic tachycardia syndrome (POTS, a condition where the heart rate increases abnormally after sitting or standing up, causing symptoms such as dizziness and fainting, as well as headache, chest pain and weakness).

Reports of these conditions in young women who have received an HPV vaccine have been previously considered during routine safety monitoring by the PRAC but a causal link between them and the vaccines was not established. Both conditions can occur in non-vaccinated individuals and it is considered important to further review if the number of cases reported with HPV vaccine is greater than would be expected.

In its review the PRAC will consider the latest scientific knowledge, including any research that could help clarify the frequency of CRPS and POTS following vaccination or identify any causal link. Based on this review, the Committee will decide whether to recommend any changes to product information to better inform patients and healthcare professionals. While the review is ongoing there is no change in recommendations for the use of the vaccine.



---

### **More about the medicine**

HPV vaccines are available in the European Union under the names Gardasil/Silgard, Gardasil 9, and Cervarix. Gardasil has been authorised since September 2006, and is approved in both males and females for preventing precancerous growths and cancer in the cervix and anus, and genital warts. It protects against 4 types of HPV (types 6, 11, 16 and 18). Gardasil 9 (approved in June 2015) is used similarly but protects against 9 types of the virus (6, 11, 16, 18, 31, 33, 45, 52 and 58). Cervarix has been approved since September 2007 for use in women and girls to protect against precancerous growths and cancer in the cervix and genital area. It is active against types 16 and 18 of the virus. Following their approval, the vaccines have been introduced in national immunisation programs in many countries worldwide.

### **More about the procedure**

The review of HPV vaccines has been initiated by the European Commission at the request of Denmark, under Article 20 of Regulation (EC) No 726/2004.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. The PRAC recommendations will then be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt a final opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.





EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

09 July 2015  
EMA/PRAC/454436/2015

## PRAC List of questions

To be addressed by the marketing authorisation holders

Article 20 of Regulation (EC) No 726/2004 resulting from pharmacovigilance data

Human papillomavirus (HPV) vaccines

Cervarix: EMEA/H/A20/1421/C/0721/0071

Gardasil: EMEA/H/A20/1421/C/0703/0060

Gardasil 9: EMEA/H/A20/1421/C/3852/0001

Silgard: EMEA/H/A20/1421/C/0732/0054

Marketing authorisation holders: GlaxoSmithKline Biologicals; Merck Sharp & Dohme Limited; Sanofi Pasteur MSD



# 1. Background

Human papillomavirus (HPV) vaccines have been authorised in Europe for prevention of cervical and various other cancers caused by HPV infection since 2006. Routine surveillance of suspected serious adverse drug reaction reports of the HPV vaccines have raised questions on the potential association between the use of the vaccines and in particular two syndromes, known as Complex Regional Pain Syndrome (CRPS) and Postural Orthostatic Tachycardia Syndrome (POTS).

The vast majority of the reported cases do not have a well-defined diagnosis. The need was identified that overall scientific evidence of a potential association between HPV vaccination and the two syndromes should be reviewed and methodologies to further investigate the concerns should be defined, if appropriate. In addition, discussion is needed on whether there is evidence of a causal association between HPV vaccination and CRPS and/or POTS, if research efforts should be strengthened, and if available information may require updates to the advice to healthcare professionals and patients, including changes to product information or other regulatory measures.

In that respect the marketing authorisation holders (MAHs) are requested to respond to the following questions.

## 2. Questions

### Question 1

The MAHs should provide a cumulative review of available data from clinical trials, post-marketing and literature in order to evaluate the cases of CRPS and POTS with their product.

Review and case detection methods should be clearly described and the evaluation should discuss whether the reported cases fulfil published or recognised diagnostic criteria.

### Question 2

Please provide an in depth review of cases of CRPS and POTS observed within all clinical studies; with comparison of HPV vaccine groups and control groups. If differences are observed, please discuss potential explanations including risk factors for the development of CRPS and POTS.

### Question 3

The MAHs should provide an analysis of the observed number of post-marketing cases of CRPS and POTS in association with their HPV vaccine in comparison to those expected in the target population, stratified by region, if available. The analysis should discuss the assumptions made with respect to the background incidence in the target population and also the influence of potential under-reporting of cases in association with HPV vaccines.

### Question 4

The MAHs should provide a critical appraisal of the strength of evidence for a causal association with HPV vaccine for CRPS and POTS. This should consider the available published literature, including epidemiological studies, and also the possible causes and pathophysiology of CRPS and POTS and discuss whether there is biological basis for a possible causal association.

### Question 5

The MAHs should discuss the need for possible risk minimisation tools and provide proposals as appropriate.



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

13 July 2015  
EMA/PRAC/454661/2015

## Timetable for the procedure

Article 20 of Regulation (EC) No 726/2004 resulting from pharmacovigilance data

Human papillomavirus (HPV) vaccines

Cervarix: EMEA/H/A20/1421/C/0721/0071

Gardasil: EMEA/H/A20/1421/C/0703/0060

Gardasil 9: EMEA/H/A20/1421/C/3852/0001

Silgard: EMEA/H/A20/1421/C/0732/0054

Procedural step:	Date
Notification:	09 July 2015
Start of the procedure (PRAC):	July 2015 PRAC
List of questions:	09 July 2015
Submission of responses:	20 August 2015
Re-start of the procedure:	27 August 2015
Rapporteur/co-rapporteur assessment reports circulated to PRAC and to CHMP <sup>1</sup>	25 September 2015
Comments:	01 October 2015

<sup>1</sup> Committee for Medicinal Products for Human Use



<b>Procedural step:</b>	<b>Date</b>
PRAC list of questions to Scientific advisory group	October 2015 PRAC
Scientific advisory group (SAG)	Exact date to be confirmed
Updated Rapporteur/co-rapporteur assessment reports circulated to PRAC and to CHMP	28 October 2015
PRAC list of outstanding issues or PRAC recommendation to CHMP	November 2015 PRAC

**NOTIFICATION TO THE PRAC/EMA SECRETARIAT OF A  
REFERRAL UNDER ARTICLE 20 OF REGULATION (EC) 726/2004**

**E-mail:** [ReferralNotifications@ema.europa.eu](mailto:ReferralNotifications@ema.europa.eu)

This notification is a referral under Article 20 of Regulation (EC) 726/2004 to the PRAC made by the European Commission:

Product Name(s)	- Cervarix (Bivalent HPV vaccine (types 16, 18)
Procedure name	- Gardasil (quadrivalent HPV vaccine (types 6, 11, 16, 18)
HPV vaccines	- Gardasil 9 (9-valent HPV vaccine (types 6, 11, 16, 18, 31, 33, 45, 52 and 58)
	- Silgard (quadrivalent HPV vaccine (types 6, 11, 16, 18)
Active Substance(s)	All
Pharmaceutical form(s)	All
Strength(s)	All
Route of administration(s)	All
Marketing Authorisation Holder(s)	GlaxoSmithKline Biologicals S.A.  Merck Sharp & Dohme LTD  Sanofi Pasteur MSD, SNC

Human papillomavirus (HPV) vaccines have been authorised in Europe for prevention of cervical and various other cancers caused by HPV infection since 2006. Following approval, these vaccines have been introduced in national immunisation programs worldwide, including in most EU member states.

The efficacy and safety of these medicinal products has been clearly demonstrated and the benefit of these vaccines in protecting against HPV related diseases is well established. Since launch, approximately 55 million subjects are estimated to have been vaccinated with Gardasil worldwide. Cumulative marketing exposure to Cervarix is estimated as being around 17 million subjects worldwide.

Routine surveillance of suspected serious adverse drug reaction reports have raised questions on the potential association between the use of the vaccines and two syndromes in particular, which are known as Complex Regional Pain Syndrome (CRPS) and Postural Orthostatic Tachycardia Syndrome (POTS). The vast majority of the reported cases do not have a well-defined diagnosis. These syndromes have been reviewed repeatedly by the PRAC within routine safety follow up procedures, and a relationship with vaccination has not been established in these previous procedures.

For CRPS most common symptoms are severe pain, swelling and changes in the skin temperature and colour of the arms or legs, but may also include amongst other symptoms headache, general fatigue, coldness of the legs, limb pain and weakness. POTS is characterised by an abnormally large increase in heart rate when changing from a lying down to a standing up position, without any orthostatic hypotension. In POTS, this excessive heart rate increase may be accompanied by a range of symptoms which may include light headedness, visual blurring, palpitations, tremulousness and weakness (especially of the legs), as well as fatigue, shortness of breath, chest pain, concentration difficulties, and headaches.

Individual case reports and case series of CRPS and POTS have been reported in the literature following HPV vaccination from several geographically distinct locations. Literature reports of CRPS come from Australia, Germany and Japan and reports of POTS originate from USA, Japan and Denmark.

The Danish Health and Medicines Authority drew the attention of the EMA and the Commission to the issue mentioned above in July 2015. It considers that in view of the seriousness and increasing number of reports and publications raising concern in EU Member States, this safety issue should be evaluated to ensure that sufficient scientific knowledge on the potential relationship is established.

There are uncertainties regarding the underlying pathogenesis for CRPS and POTS and an association between HPV vaccination and CRPS or POTS has also not been established. These conditions have been well known for a long time and before the introduction of the HPV vaccines.

It is recognised that these conditions can occur in the general non-vaccinated population and it is considered important to undertake further review to determine whether the number of cases reported with HPV vaccine is greater than would ordinarily be expected.

The Danish Health and Medicines Authority underlined that the objective with HPV vaccination is to prevent serious life-threatening disease, the exposure of healthy individuals

to the vaccine is extensive, the risk-benefit balance should be favourable and the risks effectively monitored and well characterized.

The persisting uncertainty with regard to causal association between CRPS/POTS and HPV vaccination may have a significant impact on the future confidence in national vaccination programs.

Overall scientific evidence of a potential association between HPV vaccination and the two syndromes should be reviewed and methodologies to further investigate the concerns should be defined, if appropriate.

In view of the above, the European Commission (EC) initiates a procedure under Article 20 of Regulation (EC) No 726/2004 and requests the Agency to assess the above concerns for the centrally authorised medicinal product(s) (mentioned above). The EC requests the Agency to give its opinion as soon as possible and not later than 31 May 2016 on whether there is evidence of a causal association between HPV vaccination and CRPS and/or POTS, and if available information may require updates to the advice to healthcare professionals and patients, including changes to product information or other regulatory measures on the marketing authorisations concerned.

As the request results from the evaluation of data resulting from pharmacovigilance activities, the opinion should be adopted by the Committee for Medicinal Products for Human Use on the basis of a recommendation of the Pharmacovigilance Risk Assessment Committee.



*917/2015*

Sabine Jülicher

Head of Unit

European Commission

DG Health and Food Safety

Unit D5 - Medicinal products - authorisations, European Medicines Agency

**From:** Kuter, Barbara J.  
**Sent:** Mon, 2 Nov 2015 17:47:07 -0500  
**To:** Markowitz, Lauri (CDC/OID/NCIRD);Destefano, Frank (CDC/OID/NCEZID);Wharton, Melinda (CDC/OID/NCIRD)  
**Subject:** HPV referral (EMA Article 20) - CRPS & POTS - CONFIDENTIAL

Lauri, Frank & Melinda,

I am sending this note to give you a heads-up that we are expecting a positive recommendation from the Pharmacovigilance Risk Assessment Committee (PRAC) of the EMA/CHMP to conclude the referral that was conducted regarding the safety of HPV vaccines under Article 20. As you know, the PRAC was reviewing data on CRPS & POTS following HPV vaccination & it is our understanding that they have not found anything of concern. We have been informed that the PRAC is planning to have their Public Health Communication released to the public on Thursday, Nov 5<sup>th</sup>.

I will send along the notice as soon as it is received.

Please handle this information as CONFIDENTIAL until released.

Thanks.

Barb

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



**From:** Debora Rausch  
**Sent:** Thu, 22 Feb 2018 14:43:47 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID);Shimabukuro, Tom (CDC/OID/NCEZID);McNeil, Michael (CDC/OID/NCEZID);Weintraub, Eric (CDC/OID/NCEZID);Broder, Karen (CDC/OID/NCEZID);Wodi, Akpobome (CDC/OID/NCEZID);Harrington, Theresa (CDC/OID/NCEZID);Stanfill, Katherine (CDC/OID/NCEZID) (CTR);zqg1@cdc.gov;Grohskopf, Lisa A. (CDC/OID/NCIRD);Dooling, Kathleen L. (CDC/OID/NCIRD);Harpaz, Rafael (CDC/OID/NCIRD);Miller, Elaine R. (CDC/OID/NCEZID);Wharton, Melinda (CDC/OID/NCIRD);Cohn, Amanda (CDC/OID/NCIRD);dcn4@cdc.gov;nelson.jl@ghc.org;belongia.edward@marshfieldresearch.org;jackson.l@ghc.org;jackson.ml@ghc.org;ned.lewis@kp.org;Nicola.Klein@kp.org;kenneth.schmader@duke.edu;ktalaat@jhu.edu;Mary.Staat@cchmc.org;Elizabeth.Schlaudecker@cchmc.org;psl1@cumc.columbia.edu;aa g1@cumc.columbia.edu;chip.walter@duke.edu;geeta.swamy@duke.edu;Neal Halsey  
**Cc:** Cara Crumlish  
**Subject:** GSK Presentation of Shingrix Post Licensure Safety Plans to CDC ISO and Partners (Presentation Attached)

Good Morning,  
Please find attached the GSK Shingrix post-licensure safety monitoring presentation for tomorrow, Friday, February 23<sup>rd</sup> 2018 , 11 AM EST.  
You should already have a calendar invite for this date and time.  
In the event that you do not, please find the dial-in details below.  
Please note, that we are required to conduct a quick attendance check concordant with already received CDAs.  
To ensure a prompt start to the meeting, we would appreciate if participants begin to call in at 10:55 am.  
Thank you,  
Debora Rausch MD MA

## Dial In Details

	Debora Rausch
Name:	
Chairperson passcode:	
Participant passcode:	
GSK VPN number:	
USA toll (local dial-in):	
USA toll-free:	
UK toll (local dial-in):	
UK toll-free:	
Belgium (local dial-in):	
Belgium toll-free:	

(b)(6)

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

**From:** Cristina Masseria  
**Sent:** Fri, 10 Jan 2014 21:20:12 +0000  
**To:** Clark, Thomas A. (CDC/OID/NCIRD); Destefano, Frank (CDC/OID/NCEZID); Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID); Liang, Jennifer L. (CDC/OID/NCIRD); Linda Hanssens  
**Subject:** RE: [REDACTED] (b)(4)

Dear Frank,

My plan is to send you a brief concept document by the 16.

From GSK these are the people attending:  
Leonard Silverstein (US Medical Affairs for pertussis),  
Linda Hanssens (Global Medical Affairs Lead for pertussis),  
Shanthi Krishnarajah (US Vaccines Health Outcomes and Epidemiology lead)  
and myself.

Thank you and best regards,  
Cristina

---

**From:** Clark, Thomas A. (CDC/OID/NCIRD) [mailto:tnc4@cdc.gov]  
**Sent:** Friday, January 10, 2014 4:11 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Cristina Masseria; Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID); Liang, Jennifer L. (CDC/OID/NCIRD)  
**Subject:** RE: [REDACTED] (b)(4)

Thanks. yes, we'll plan to join.

---

**From:** Destefano, Frank (CDC/OID/NCEZID)  
**Sent:** Thursday, January 09, 2014 12:00 PM  
**To:** Cristina Masseria; Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Liang, Jennifer L. (CDC/OID/NCIRD)  
**Subject:** RE: [REDACTED] (b)(4)

That sounds good. It would be helpful if we could receive a brief concept document that we could review before the meeting. Please let me know who from GSK will be attending so that we can arrange suitable meeting space.

Thanks,  
Frank

P.S. Tom and Jennifer – You are welcome to attend if you are available.

---

**From:** Cristina Masseria [<mailto:cristina.x.masseria@gsk.com>]  
**Sent:** Thursday, January 09, 2014 10:40 AM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: [REDACTED] (b)(4)

Dear Dr De Stefano,

1-2 is good for us.

Regarding the logistics, Jennifer Liang and Renalda Barlatier are organizing our CDC passes. I am going to find out if it is ok for us to stay until 2 or if we need an extension.

We are at the moment working on the concept protocol for the GSK safety study and, if you agree, I would like to send you the document before the meeting (one week in advance) to facilitate our discussion.

Thank you again for your availability.

Best regards  
Cristina

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Wednesday, January 08, 2014 5:08 PM  
**To:** Cristina Masseria; Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: [REDACTED] (b)(4)

Ideally, we would prefer to meet with you during the 9-12 pm meeting with Dr. Clark's group, but unfortunately Dr. Broder and I are not available that morning. Would you and your colleagues be able to stay on for a separate meeting with us from 1-2 pm that day?

Thanks,  
Frank

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**Sent:** Tuesday, January 07, 2014 9:36 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: [REDACTED] (b)(4)

Thank you for your flexibility.

Do you prefer to set up a separate meeting or to have our discussion during the 9-12pm meeting with Dr Clark and his colleagues?

I am still working on the final agenda. We have 3 hours and therefore there should be enough time to cover both epidemiology/health economics studies and safety studies in case you prefer the second option.



Best regards,  
Cristina

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Tuesday, January 07, 2014 4:30 PM  
**To:** Cristina Masseria; Shanthy Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Sorry that we got the date wrong. I have some availability on 1/23.

Thanks,  
Frank

---

**From:** Cristina Masseria [<mailto:cristina.x.masseria@gsk.com>]  
**Sent:** Tuesday, January 07, 2014 4:11 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Shanthy Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Dear Dr De Sterfano,

That's great news. However, the meeting with Dr Clark is scheduled for January 23<sup>rd</sup> from 9-noon and not for the 22<sup>nd</sup>. Sorry for the confusion.

Are you and Dr Broder available for January 23<sup>rd</sup>?

Thank you and happy New Year,  
Cristina

***Cristina Masseria, PhD***  
***GlaxoSmithKline***  
***US Health Outcomes and Medical Policy - Vaccines***  
***Phone: +1.215.751.4960***

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Tuesday, January 07, 2014 3:53 PM  
**To:** Shanthy Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Cristina Masseria; Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Dear Ms. Krishnarajah,

Thank you again for your request for consultation and for your patience in waiting for our response. We have a mutual interest in gaining more data on (b)(4)

(b)(4)

Dr. Broder and I could be available to meet with GSK colleagues to discuss (b)(4)

(b)(4)

in January 22 when you are at CDC. Dr. Cindy Weinbaum, in the Division of Healthcare

Quality Promotion (copied here), will follow-up with you in the near future on the logistics for the safety meeting. We can further discuss your other questions during that time.

Best wishes for the New Year,

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA

---

**From:** Shanthi Krishnarajah [<mailto:girishanthi.x.krishnarajah@gsk.com>]  
**Sent:** Monday, December 16, 2013 10:15 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Cristina Masseria; Leonard Silverstein  
**Subject:** RE: Safety of Boostrix during pregnancy

Dear Dr. Destefano and Dr. Broder,

Thank you for your time on Dec 5<sup>th</sup> call.

(b)(4)

We are still in the process of drafting a concept design and would like to see if you would be open to reviewing the protocol.

And finally we are having a face to face meeting with Tom and his colleagues the morning of Jan 22<sup>nd</sup>. Let us know if you would also be open to meeting us that day.

Thanks very much and Happy Holidays

Shanthi Krishnarajah, MPH, MBA/MS  
Head US HO/Epidemiology Vaccines

USHO and MP  
Work Tel: 215 751-3267  
Cell : 610 213 3740

Pls Note my new office number

**From:** Cristina Masseria  
**Sent:** Fri, 10 Jan 2014 18:20:15 +0000  
**To:** Liang, Jennifer L. (CDC/OID/NCIRD);Shanthi Krishnarajah  
**Cc:** Cho, Bo-Hyun (CDC/OID/NCIRD);Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: Agenda for January meeting

Hi Jennifer,

I was just about to send you an email with the updated agenda.

(b)(4)

Best,  
Cristina

***Cristina Masseria, PhD***  
***GlaxoSmithKline***  
***US Health Outcomes and Medical Policy - Vaccines***  
***Phone: +1.215.751.4960***



---

**From:** Liang, Jennifer L. (CDC/OID/NCIRD) [mailto:bgz8@cdc.gov]  
**Sent:** Friday, January 10, 2014 1:12 PM  
**To:** Cristina Masseria; Shanthi Krishnarajah  
**Cc:** Cho, Bo-Hyun (CDC/OID/NCIRD)  
**Subject:** Agenda for January meeting

Hi Cristina and Shanthi,

I just wanted to check if there are others we should invite from our Branch to this meeting.

I don't recall us discussing a specific agenda (yet). I have the following:

(b)(4)

Thanks,  
Jennifer

---

**From:** Destefano, Frank (CDC/OID/NCEZID)  
**Sent:** Thursday, January 09, 2014 12:00 PM  
**To:** Cristina Masseria; Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Liang, Jennifer L. (CDC/OID/NCIRD)  
**Subject:** RE [REDACTED] (b)(4)

That sounds good. It would be helpful if we could receive a brief concept document that we could review before the meeting. Please let me know who from GSK will be attending so that we can arrange suitable meeting space.

Thanks,

Frank

P.S. Tom and Jennifer – You are welcome to attend if you are available.

---

**From:** Cristina Masseria [<mailto:cristina.x.masseria@gsk.com>]  
**Sent:** Thursday, January 09, 2014 10:40 AM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Dear Dr De Stefano,

1-2 is good for us.

Regarding the logistics, Jennifer Liang and Renalda Barlatier are organizing our CDC passes. I am going to find out if it is ok for us to stay until 2 or if we need an extension.

We are at the moment working on the concept protocol for the GSK safety study and, if you agree, I would like to send you the document before the meeting (one week in advance) to facilitate our discussion.

Thank you again for your availability.

Best regards  
Cristina

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Wednesday, January 08, 2014 5:08 PM  
**To:** Cristina Masseria; Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

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Thanks,  
Frank

---

**From:** Cristina Masseria [<mailto:cristina.x.masseria@gsk.com>]  
**Sent:** Tuesday, January 07, 2014 9:36 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Thank you for your flexibility.

Do you prefer to set up a separate meeting or to have our discussion during the 9-12pm meeting with Dr Clark and his colleagues?

I am still working on the final agenda. We have 3 hours and therefore there should be enough time to cover both epidemiology/health economics studies and safety studies in case you prefer the second option.

Best regards,  
Cristina

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Tuesday, January 07, 2014 4:30 PM  
**To:** Cristina Masseria; Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: [REDACTED] (b)(4)

Sorry that we got the date wrong. I have some availability on 1/23.  
Thanks,  
Frank

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**Sent:** Tuesday, January 07, 2014 4:11 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: [REDACTED] (b)(4)

Dear Dr De Sterfano,

That's great news. However, the meeting with Dr Clark is scheduled for January 23<sup>rd</sup> from 9-noon and not for the 22<sup>nd</sup>. Sorry for the confusion.

Are you and Dr Broder available for January 23<sup>rd</sup>?

Thank you and happy New Year,  
Cristina

***Cristina Masseria, PhD***  
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**To:** Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Cristina Masseria; Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: [REDACTED] (b)(4)

Dear Ms. Krishnarajah,

Thank you again for your request for consultation and for your patience in waiting for our response. We have a mutual interest in gaining more data (b)(4)

(b)(4) Dr. Broder and I could be available to meet with GSK colleagues to discuss (b)(4)

(b)(4) on January 22 when you are at CDC. Dr. Cindy Weinbaum, in the Division of Healthcare Quality Promotion (copied here), will follow-up with you in the near future on the logistics for the safety meeting. We can further discuss your other questions during that time.

Best wishes for the New Year,

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA

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**From:** Shanthy Krishnarajah [<mailto:girishanthi.x.krishnarajah@gsk.com>]  
**Sent:** Monday, December 16, 2013 10:15 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Cristina Masseria; Leonard Silverstein  
**Subject:** RE: (b)(4)

Dear Dr. Destefano and Dr. Broder,

Thank you for your time on Dec 5<sup>th</sup> call.

(b)(4)

Thanks very much and Happy Holidays

Shanthy Krishnarajah, MPH, MBA/MS  
Head US HO/Epidemiology Vaccines  
USHO and MP  
Work Tel: 215 751-3267  
Cell : 610 213 3740

Pls Note my new office number



**From:** Cristina Masseria  
**Sent:** Thu, 16 Jan 2014 20:11:57 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID);Shanthy Krishnarajah;Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein;Weinbaum, Cindy (CDC/OID/NCEZID);Clark, Thomas A. (CDC/OID/NCIRD);Liang, Jennifer L. (CDC/OID/NCIRD);Linda Hanssens;Jacqueline Miller  
**Subject:** RE: (b)(4)  
**Attachments:** (b)(4)

Dear Dr De Stefano,

I have attached a brief concept document in preparation for next week meeting.

Moreover, from GSK also Jacqueline Miller will be attending the meeting.

Thank you and best regards,

Cristina

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Thursday, January 09, 2014 12:00 PM  
**To:** Cristina Masseria; Shanthy Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD); Liang, Jennifer L. (CDC/OID/NCIRD)  
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**From:** Cristina Masseria [<mailto:cristina.x.masseria@gsk.com>]  
**Sent:** Tuesday, January 07, 2014 4:11 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Dear Dr De Sterfano,

That's great news. However, the meeting with Dr Clark is scheduled for January 23<sup>rd</sup> from 9-noon and not for the 22<sup>nd</sup>. Sorry for the confusion.

Are you and Dr Broder available for January 23<sup>rd</sup>?

Thank you and happy New Year,  
Cristina

***Cristina Masseria, PhD***  
***GlaxoSmithKline***  
***US Health Outcomes and Medical Policy - Vaccines***  
***Phone: +1.215.751.4960***

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Tuesday, January 07, 2014 3:53 PM  
**To:** Shanthi Krishnarajah; Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Cristina Masseria; Leonard Silverstein; Weinbaum, Cindy (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Dear Ms. Krishnarajah,

Thank you again for your request for consultation and for your patience in waiting for our response. We have a mutual interest in gaining more data on the (b)(4)

(b)(4) Dr. Broder and I could be available to meet with GSK colleagues to discuss (b)(4)

(b)(4) on January 22 when you are at CDC. Dr. Cindy Weinbaum, in the Division of Healthcare Quality Promotion (copied here), will follow-up with you in the near future on the logistics for the safety meeting. We can further discuss your other questions during that time.

Best wishes for the New Year,

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA



---

**From:** Shanthi Krishnarajah [<mailto:girishanthi.x.krishnarajah@gsk.com>]  
**Sent:** Monday, December 16, 2013 10:15 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID); Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Cristina Masseria; Leonard Silverstein  
**Subject:** RE: (b)(4)

Dear Dr. Destefano and Dr. Broder,

Thank you for your time on Dec 5<sup>th</sup> call.

(b)(4)

Thanks very much and Happy Holidays

Shanthi Krishnarajah, MPH, MBA/MS  
Head US HO/Epidemiology Vaccines  
USHO and MP  
Work Tel: 215 751-3267  
Cell : 610 213 3740

Pls Note my new office number

Topics for discussion pertaining to the feasibility of safety studies o

(b)(4)

(b)(4)

(b)(4)

- Would CDC be willing to review our protocol with the CDC-run study to ensure consistency and comparability?
- Any lesson learnt in the setting up of the study with your sites that we can implement
- Thoughts re: an appropriate control arm for the study and length of follow up for mothers and infants

**From:** Dr.Johnson@sanofipasteur.com  
**Sent:** Sun, 3 Feb 2013 15:34:38 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Michael.Decker@sanofipasteur.com;David.Greenberg@sanofipasteur.com; (b)(4)  
(b)(4);Kristen.Sharma@sanofipasteur.com;Vellozzi, Claudia (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Frank:

I was able to check with our PV colleagues who oversee the (b)(4)

(b)(4)

(b)(4)

I hope this information is useful for you.

If you intend to present at the Feb 20-21 ACIP meeting any slides that refer to the (b)(4)  
(b)(4) we would be more than happy to preview these, provide you feedback on them, and do so with the understanding that the slides are confidential until presented at the ACIP meeting..

David

---

**From:** Johnson, Dr. David R. (sanofi pasteur)  
**Sent:** Wednesday, January 30, 2013 10:12 PM  
**To:** 'Destefano, Frank (CDC/OID/NCEZID)'  
**Cc:** Vellozzi, Claudia (CDC/OID/NCEZID); Greenberg, David (sanofi pasteur); (b)(4)  
(b)(4)  
**Subject:** RE: (b)(4)

Hello Frank:

I will check on this with our pharmacovigilance colleagues who manage the registry and then get back with you promptly.

Best wishes,

David

**David R. Johnson, MD, MPH**  
Vice President and Regional Medical Expert  
Sanofi Pasteur, Swiftwater, Pennsylvania  
office phone: +1 570 957 1506 mobile phone: +1 570 350 2098  
e-mail: dr.johnson@sanofipasteur.com

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Wednesday, January 30, 2013 3:31 PM  
**To:** (b)(4)

**Cc:** Vellozzi, Claudia (CDC/OID/NCEZID); Johnson, Dr. David R. (sanofi pasteur); Greenberg, David (sanofi pasteur)

**Subject:** RE: (b)(4)

Phil,

Thanks for making this connection with Dr. Johnson. As I mentioned, we were just curious if the recommendation to (b)(4)

(b)(4)

Thanks again,  
Frank

---

**From:** (b)(4)

**Sent:** Wednesday, January 30, 2013 2:22 PM

**To:** Destefano, Frank (CDC/OID/NCEZID)

**Cc:** Vellozzi, Claudia (CDC/OID/NCEZID); Dr.Johnson@sanofipasteur.com;  
David.Greenberg@sanofipasteur.com

**Subject:** RE: (b)(4)

Frank,

The person who can best help you with Sanofi Pasteur (b)(4)  
whom I have copied here.

Best Regards,

(b)(4)

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]

**Sent:** Wednesday, January 30, 2013 12:02 PM

**To:** (b)(4)

**Cc:** Vellozzi, Claudia (CDC/OID/NCEZID)

**Subject:** Tdap in pregnancy registry

Hi (b)(4)

I was informed by Tom Clark that you are the contact for (b)(4) This is just a heads up that I will be presenting at the February ACIP meeting on our plans for monitoring safety of

(b)(4)

(b)(4)

Thanks and best regards,  
Frank

Frank DeStefano, MD, MPH  
Director

Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA

\*\*\*\*\*

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\*\*\*\*\*

**From:** (b)(4)  
**Sent:** Wed, 30 Jan 2013 17:32:45 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Vellozzi, Claudia (CDC/OID/NCEZID)  
**Subject:** RE: (b)(4)

Dear Frank,

Thanks for the heads-up. I'll let our US people know, so they can be prepared.

(b)(4)

Best regards,

(b)(4)

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Wednesday, January 30, 2013 12:00 PM  
**To:** Harry Seifert  
**Cc:** Vellozzi, Claudia (CDC/OID/NCEZID)  
**Subject:** (b)(4)

Hi

(b)(4)

I was informed by Jennifer Liang that you are one of the contacts for

(b)(4)

(b)(4)

(b)(4)

Thanks and best regards,  
Frank

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA

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

Dear Frank:

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

Kind regards,  
Peggy

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

5952 Trippe Creek Drive  
Oxford, MD 21654

202-286-4025 (cell)  
410-770-3686



**From:** David Vaughn  
**Sent:** Mon, 17 Nov 2014 21:04:30 +0000  
**To:** Broder, Karen (CDC/OID/NCEZID);Fernanda Tavares Da Silva;Valentina Attanasi;François P Roman;Destefano, Frank (CDC/OID/NCEZID);Gronostaj, Michael (CDC/OID/NCEZID);Clark, Thomas A. (CDC/OID/NCIRD)  
**Subject:** RE: CDC-GSK Phase 3 and post-licensure PV  
**Attachments:** CDC Ebola vaccine study - draft AEFI\_Prevention Form 11 10 14-3pm[1] dv.docx

Karen,

See attached or two comments. Talk to you on Thursday. David.

---

**From:** Broder, Karen (CDC/OID/NCEZID) [mailto:krb2@cdc.gov]  
**Sent:** Friday, November 14, 2014 11:22 AM  
**To:** David Vaughn; Fernanda Tavares Da Silva; Valentina Attanasi; François P Roman; Destefano, Frank (CDC/OID/NCEZID); Gronostaj, Michael (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD)  
**Subject:** RE: CDC-GSK Phase 3 and post-licensure PV

David and Colleagues,

Here is the other draft AEFI prevention form. There is a section in yellow that would be good to update for accuracy re the GSK vaccine.

I am working on getting some schedule info from the CDC folks and will get back to David with some potential times for continued discussion.  
Stay warm.

Thanks,  
Karen

-----Original Appointment-----

**From:** David Vaughn [mailto:david.w.vaughn@gsk.com]  
**Sent:** Friday, November 07, 2014 3:26 PM  
**To:** David Vaughn; Fernanda Tavares Da Silva; Valentina Attanasi; François P Roman; Destefano, Frank (CDC/OID/NCEZID); Gronostaj, Michael (CDC/OID/NCEZID); Broder, Karen (CDC/OID/NCEZID); Clark, Thomas A. (CDC/OID/NCIRD)  
**Subject:** CDC-GSK Phase 3 and post-licensure PV  
**When:** Friday, November 14, 2014 10:00 AM-11:00 AM (UTC-05:00) Eastern Time (US & Canada).  
**Where:** TC - see below

When: Friday, November 14, 2014 10:00 AM-11:00 AM (UTC-05:00) Eastern Time (US & Canada).  
Where: TC - see below

Note: The GMT offset above does not reflect daylight saving time adjustments.

\*~\*~\*~\*~\*~\*~\*~\*~\*~\*

TC Details

Belgium Toll access n: (b)(6)

Belgium Toll-free access n: (b)(6)

Canada Toll access n: + (b)(6)

Canada Toll-free access n: (b)(6)

US Toll-free access n: (1) (b)(6)

Participant code (b)(6)

Ebola Candidate Vaccine Evaluation: Adverse Events Following  
Immunization (AEFI) Prevention Form -- DRAFT

---

(b)(4)

Ebola Candidate Vaccine Evaluation: Adverse Events Following  
Immunization (AEFI) Prevention Form -- DRAFT

(b)(4); (b)(5)

Ebola Candidate Vaccine Evaluation: Adverse Events Following  
Immunization (AEFI) Prevention Form -- DRAFT

(b)(4); (b)(5)

**From:** David Vaughn  
**Sent:** Fri, 16 Jan 2015 22:22:58 +0000  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID); Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: IBM Citizen Engagement Program in Sierra Leone  
**Attachments:** 2014 12 22 IBM-GSK TC.pdf, 2015 01 15 IBM-GSK TC.pdf

Karen,

Thanks. I have attached summaries from our two calls with IBM. Francois Roman is traveling to SL on Sunday. It could be a good time to discuss while Francois and Marc-Alain are both in SL. Let me know if any interest to consider a supplemental approach to acquiring safety data for your phase 3 and I will try to set up a call. If no interest for SL, then right, no urgency. David.

---

**From:** Broder, Karen (CDC/OID/NCEZID) [mailto:krb2@cdc.gov]  
**Sent:** Friday, January 16, 2015 4:17 PM  
**To:** David Vaughn  
**Cc:** Gronostaj, Michael (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID); Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: IBM Citizen Engagement Program in Sierra Leone

Hi David,

Thanks for the update. Our Immunization Safety Office (ISO) team has general interest in learning more about this smart phone app for PV use in developing countries. This is not time urgent and if we do this I could work with you to coordinate an educational update at a convenient time, unrelated to the study timeline.

The Ebola Vaccine Team Lead, Marc-Alain, involved with this area is in the field in SL now and we aren't sure what he'll be available to review this issue. We have passed along your kind email and will let you know if we hear anything back regarding your query.

Have a good weekend.

Karen

---

**From:** David Vaughn [mailto:david.w.vaughn@gsk.com]  
**Sent:** Thursday, January 15, 2015 12:26 PM  
**To:** Broder, Karen (CDC/OID/NCEZID)  
**Subject:** IBM Citizen Engagement Program in Sierra Leone  
**Importance:** High

Karen,

Do you have a few minutes for a phone call? We are talking with IBM. They have set up a call center in Sierra Leone related to Ebola. They also have a capacity to supply smart phones with specific apps within a few week. We thought you might be interested in a secondary approach to collecting safety

(b)(4)

**David W. Vaughn, MD, MPH**

Head, External R&D, North America  
Vaccines Discovery & Development

**GSK**

2301 Renaissance Boulevard, RN0220

King of Prussia, PA 19406-2772, USA

**Email** [David.W.Vaughn@gsk.com](mailto:David.W.Vaughn@gsk.com)

**Tel** +1 610-917-4898 (GSK internal 8-202-4898)

**Mobile** +1 267-355-2160

**Admin. Support** Elaine Slavish +1 610-917-4433

*For collaboration proposal:* [VaccinesPartnering@gsk.com](mailto:VaccinesPartnering@gsk.com)

*For support request:* <https://iss.gsk.com/default.aspx>

[gsk.com](http://gsk.com) | [Twitter](#) | [YouTube](#) | [Facebook](#) | [Flickr](#)



(b)(4)



(b)(4)

(b)(4)

(b)(4)

1

**From:** MERCK  
**Sent:** Fri, 13 Nov 2020 15:03:57 +0000  
**To:** Destefano, Frank (CDC/DDID/NCEZID/DHQP)  
**Subject:** Sample our quality FBS and see the difference

## Too vital to take for granted.

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Best regards,  
Your Merck Team



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**From:** MERCK  
**Sent:** Wed, 18 Nov 2020 14:02:52 +0000  
**To:** Destefano, Frank (CDC/DDID/NCEZID/DHQP)  
**Subject:** 20% Off Glycoenzymes: Make Your Glycoprotein Research Sweeter



## Carb Up Your Research

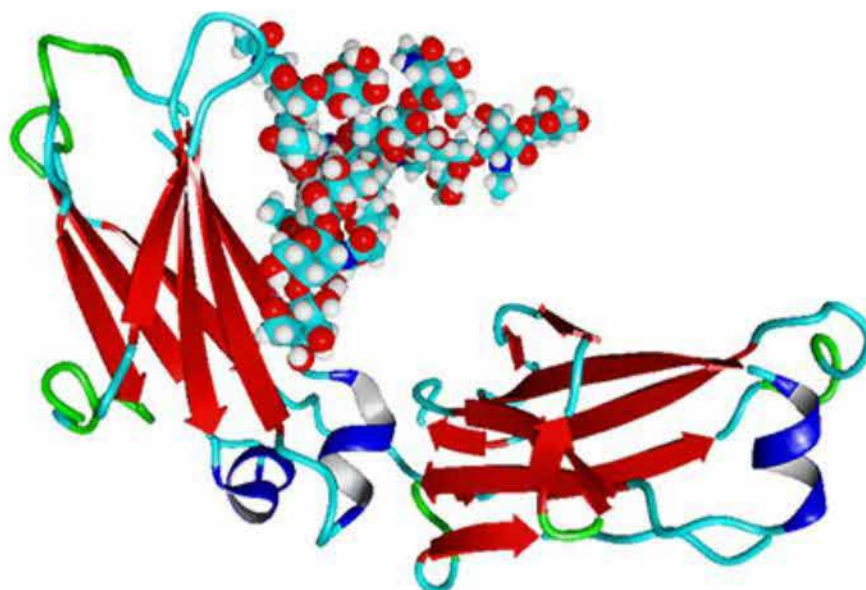
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**From:** Luis Romano  
**Sent:** Tue, 1 Dec 2020 18:49:29 +0000  
**To:** Destefano, Frank (CDC/DDID/NCEZID/DHQP);Grohskopf, Lisa A.  
(CDC/DDID/NCIRD/ID)  
**Subject:** Stock management and expired vaccine

Dear Lisa and Frank,

I hope you and your families are doing well

I bring this to your attention as CDC may want to consider reminding providers of the importance of stock management to mitigate vaccination errors.

(b)(4)

Thanks!

Best

Luis, on behalf of the GSK Flu Medical Team

**Luis Romano, MD**  
**Medical Affairs Lead, Vaccines**  
Influenza, RSV Mat/Ped and Above Brand Strategy

**GSK**

5 Crescent Drive, Philadelphia, PA 19112, United States

**Email** [luis.m.romano@gsk.com](mailto:luis.m.romano@gsk.com)

**Mobile** +1 267 408 7636

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**From:** Bailey, Steven R.  
**Sent:** Wed, 10 Aug 2016 15:22:23 +0000  
**To:** Caplanusi Irina; [REDACTED] (b)(4); Zuber, Patrick (CDC who.int); Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Rago Lembit (ragol@cioms.ch); Le\_Roux Susanne; Holm Karin  
**Subject:** RE: CIOMS WG on Vaccine Safety: Progress Report on completion of Technical Collaboration Coordination  
**Attachments:** EXECUTIVE SUMMARY 08102016.docx

Irina:

Thank you for your comments. I have incorporated them in the attached. This includes feedback now from Patrick, yourself, and me.

I tend to agree there was too much detail, and I did shorten this a bit, pointing to the detail available in the guide.

Barring additional feedback, I would consider this our working draft of the executive summary.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Caplanusi Irina [mailto:Irina.Caplanusi@ema.europa.eu]  
**Sent:** Thursday, August 4, 2016 12:16 PM  
**To:** Bailey, Steven R.; [REDACTED] (b)(4) zuberp@who.int; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; fxd1@cdc.gov  
**Cc:** Rago Lembit (ragol@cioms.ch); Le\_Roux Susanne; Holm Karin  
**Subject:** RE: CIOMS WG on Vaccine Safety: Progress Report on completion of Technical Collaboration Coordination

Dear Steven,

It is great to see the almost final shape of the Guide, thank you!

I could not spend a lot of time on this, I attach some minor comments. I had the overall impression that the level of detail is a bit high in some parts (I would not keep the table for example).

Kind regards,  
Irina

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** 02 August 2016 22:08  
**To:** [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [zuberp@who.int](mailto:zuberp@who.int); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); Caplanusi Irina; 'Holm Karin'  
**Cc:** Rago Lembit ([ragol@cioms.ch](mailto:ragol@cioms.ch)); Le\_Roux Susanne; Holm Karin  
**Subject:** CIOMS WG on Vaccine Safety: Progress Report on completion of Technical Collaboration Coordination  
**Importance:** High

Dear Editorial Board:

Sharing with you the latest version of the Guide. It is, for all intents and purposes, complete. Some additional style work is being done to prepare it for printing, and CIOMS will be working on items such as pricing, communications, etc. Likely we will be calling on you to review these materials as they are produced.

PLEASE NOTE: We are still awaiting comments/edits FROM YOU for the executive summary that will form the basis of some of these yet to be complete items. I am attaching the latest version, which contains edits from **Patrick** and **myself**. Please provide any further changes, as we would like to have this finalized **by Friday or latest next Monday**.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Holm Karin [<mailto:holm@cioms.ch>]  
**Sent:** Friday, July 29, 2016 10:29 AM  
**To:** Rago Lembit; Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int)); Bailey, Steven R.  
**Cc:** Le\_Roux Susanne  
**Subject:** CIOMS WG on Vaccine Safety: Progress Report on completion of Technical Collaboration Coordination

Date: 29 July 2016  
To: Lembit Rago, Patrick Zuber, Steven Bailey  
Cc: Sue le Roux  
From: Karin Holm

**RE: Progress Report on completion of Working Group Technical Collaboration Coordination**

This is a summary of where we stand on finishing the CIOMS Working Group on Vaccine Safety. I've included contacts and file names and have suggestions about how to finalize. For your convenience, I have attached the referenced files. If you have questions, do not hesitate to contact me. My personal email: [karinholm@bluewin.ch](mailto:karinholm@bluewin.ch), mob (b)(6) It's been a pleasure working with you all.

(b)(4)

(b)(4)

(b)(4)

(b)(6)



(b)(4)

(b)(4)

(b)(4)

(b)(4)

**From:** Bailey, Steven R.  
**Sent:** Tue, 2 Aug 2016 21:08:27 +0000  
**To:** Corinne.Jouquelet-Royer@sanofipasteur.com; Zuber, Patrick (CDC who.int); Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Destefano, Frank (CDC/OID/NCEZID); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); 'Holm Karin'  
**Cc:** Rago Lembit (ragol@cioms.ch); Le\_Roux Susanne; Holm Karin  
**Subject:** CIOMS WG on Vaccine Safety: Progress Report on completion of Technical Collaboration Coordination  
**Attachments:** Cioms guide AVSS\_master\_29\_July.docx, EXECUTIVE SUMMARY\_v1\_UH pz srb.docx  
**Importance:** High

Dear Editorial Board:

Sharing with you the latest version of the Guide. It is, for all intents and purposes, complete. Some additional style work is being done to prepare it for printing, and CIOMS will be working on items such as pricing, communications, etc. Likely we will be calling on you to review these materials as they are produced.

PLEASE NOTE: We are still awaiting comments/edits FROM YOU for the executive summary that will form the basis of some of these yet to be complete items. I am attaching the latest version, which contains edits from **Patrick** and **myself**. Please provide any further changes, as we would like to have this finalized **by Friday or latest next Monday**.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** Friday, July 29, 2016 10:29 AM  
**To:** Rago Lembit; Zuber, Patrick (zuberp@who.int); Bailey, Steven R.  
**Cc:** Le\_Roux Susanne  
**Subject:** CIOMS WG on Vaccine Safety: Progress Report on completion of Technical Collaboration Coordination

Date: 29 July 2016  
To: Lembit Rago, Patrick Zuber, Steven Bailey  
Cc: Sue le Roux  
From: Karin Holm

**RE: Progress Report on completion of Working Group Technical Collaboration Coordination**

This is a summary of where we stand on finishing the CIOMS Working Group on Vaccine Safety. I've included contacts and file names and have suggestions about how to finalize. For your convenience, I have attached the referenced files. If you have questions, do not hesitate to contact me. My personal email: [karinholm@bluewin.ch](mailto:karinholm@bluewin.ch), mob. 079 543 1838. It's been a pleasure working with you all.

## **CIOMS WG on Vaccine Safety**

### **1) Deliverable 1: CIOMS Guide for Active Vaccine Safety Surveillance**

#### **a) Status: Guide for AVSS, approximately 85 pages.**

File: G:\UnitData\CIOMS Working Groups\WG on Vaccine Safety\CURRENT VERSION\CURRENT FINAL EDBD COMMENTS July 2016\ Cioms guide AVSS\_master\_29\_July.docx

i) Content approved by WHO and Editorial Board, includes deliverables from topic group 1 (essential vaccine information) and topic group 2 (the guide).

ii) Contact: Steven Bailey, Ed-in-Chief of report of the CIOMS WG on Vaccine Safety ,  
Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*Global Established Pharma Safety Lead, Pfizer*  
Tel. +1 484 865 3670 [Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com)

#### **b) Pending issues:**

i) Should be reviewed by Secretary-General, especially Appendix 1 on Essential Vaccine Information which describes delicate national regulatory issues and Appendix 2 on membership list, where I have highlighted stakeholder category and member inclusion issues needing S-G advice.

ii) Steven will circulate one last time to EdBd for comments and final edits, if any, for returning to CIOMS by 5 August.

iii) WHO-style editing to prepare for printing: David Bramley is not available, I have forwarded the c.v. and contacts of 6 alternatives to Sue le Roux.

iv) In Appendix II. Membership and Meetings of the CIOMS Working Group on Vaccine Safety, I still have some highlighted questions on how to describe certain organizations/stakeholders, since there could be some sensitivity.

v) In Appendix II, I still have some questions on any inactive WG members to include for political reasons. None of these individuals attended any meetings nor provided feedback to me, but they may have been active behind the scenes or provided support within their organizations (albeit invisible to us). Two possible names to consider from Steven Bailey's point of view: William Gregory and Peter Arlett. Also Bernhard Heiles of Merck definitely did preparatory work, but then never attended a meeting and sent Ashley Wivel as a replacement.

#### **vi) Executive Summary and Article Publications –**

File: G:\UnitData\CIOMS Working Groups\WG on Vaccine Safety\CURRENT VERSION\EXECUTIVE SUMMARY ARTICLES\EXECUTIVE SUMMARY\_v1\_UH pz.docx

Uli Heininger wrote this based on some drafts of chapter summaries by Frank Destefano and Scott Winiecki and Irina Caplanusi (who should also get some authorship). Steven is circulating for comments to rest of EdBd, Zuber has already added comments. It needs to be updated concerning the EVI section which I have written in Appendix 1. Uli has offered to submit to Vaccine Journal, and Brighton Collaboration Quarterly. I suggest also PLOS One, at least along with all the normal ones (BMJ, Lancet, Nature, NEMJ?).



- vii) Printers: Suggested cover color: A turquoise blue to be in the same group as Vaccine PV Definitions (which is a sky blue) Pantone 318U, Pts 1, BL 6.3, Pts 1 GR 6.3, Pts 14 87.4.
- c) Publicity and Role-out
  - i) Blurb needs to be written (could be based on Executive summary (see above I.b.iv) and sent to WHO bulletin, BMJ, Lancet, Nature, NEMJ, Vaccine, Brighton Collaboration, etc.
  - ii) Powerpoint presentations needs to be developed – especially for Ed Bd to use at upcoming conferences.
  - iii) Poster created possibly.
  - iv) Christine Maure, WHO, wants to use the manual in China next month and so could possibly be interested in contributing to this effort.
- 2) Deliverable 2: CIOMS Comprehensive Communication Guide for Vaccine Safety
  - a) Status: Written document needs finalization by key author Bahri and topic group 3 members and then CIOMS editing review and WHO input.
  - b) File: G:\UnitData\CIOMS Working Groups\WG on Vaccine Safety\CURRENT VERSION\TG3 Vaccine Safety Communication\10 TG3 Draft chapter\_11 March 2016.docx
  - c) Contact: Dr. Priya Bahri, topic group 3 leader, EMA  
Lead for EMA's pharmacovigilance guideline development (EU GVP) and risk communication.  
+44 (20) 3660 8454 [priya.bahri@ema.europa.eu](mailto:priya.bahri@ema.europa.eu)
  - d) Pending issues:
    - i) CIOMS and Zuber agreed in principle to publish the document separately to be a companion document to the Guide for AVSS, under CIOMS publishing. Support from WHO to be negotiated.
    - ii) Priya has been referring to this potential doc in some EMA work she has been doing, so the CIOMS guide could be cross-referenced throughout European initiatives.
    - iii) Bruce Hugman from UMC contributed and Ken Hartigan-Go is very interested in it as well.
- 3) Requested Deliverable: private sector – regulatory information exchange and dialogue
  - a) File: G:\UnitData\CIOMS Working Groups\WG on Vaccine Safety\CURRENT VERSION\PUBLIC-PRIVATE INTERACTION \ symposium proposal on private-public interaction srb\_9june.docx
  - b) Zuber is exploring with Mike Ward of DCVRN who though could be a good topic for discussion at the spring 2017 meeting. There is no venue yet identified but it is usually in one of the member states (Brazil, Cuba, India, Indonesia, Islamic Republic of Iran, People's Republic of China, Republic of Korea, South Africa and Thailand).

**Karin R. Holm**

Technical Collaboration Coordinator, CIOMS WG on Vaccine Safety  
 CIOMS IX Risk Minimisation and CIOMS X Meta-Analysis  
 Council for International Organizations of Medical Sciences (CIOMS)  
 c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
 Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)

Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

Associate partner of UNESCO  
 In official relations with WHO

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**From:** Bailey, Steven R.  
**Sent:** Fri, 17 Jun 2016 13:00:13 +0000  
**To:** Zuber, Patrick (CDC who.int);Corinne.Jouquelet-Royer@sanofipasteur.com;novilia@biofarma.co.id;Paulo.santos@bio.fiocruz.br  
**Cc:** Irina.Caplanusi@ema.europa.eu;Destefano, Frank (CDC/OID/NCEZID);Holm Karin (holmk@cioms.ch);Winiecki, Scott (FDA/CBER);Rago Lembit (ragol@cioms.ch);Abdoellah, Siti (alt) (b)(6);Bachtiar, Novilia (novilia@biofarma.co.id);Bahri, Priya (Priya.Bahri@ema.europa.eu);Bailey, Steven R.;Bergman, Ulf (b)(6);Bruce Hugman;BUTLER, Robb;Chandler, Rebecca (alt) (rebecca.chandler@who-umc.org);Gunale, Bhagwat (alt) (bhagwat.gunale@seruminstitute.com);Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com);Keller-Stanislawski (Brigitte.Keller-Stanislawski@pei.de);Kilpi, Terhi (terhi.kilpi@thl.fi);Lindquist, Marie (Marie.Lindquist@who-umc.org);Maure, Christine (maurec@who.int);Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br);Mentzer, Dirk (Dirk.Mentzer@pei.de);Nohynek Anna (Hanna.Nohynek@thl.fi);Oberle, Doris (alt2) (Doris.Oberle@pei.de);Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br);Seifert, Harry (Harry.A.Seifert@gsk.com);Shimabukuro, Tom (CDC/OID/NCEZID);Tebaa, Amina (b)(6);Zuber, Patrick (CDC who.int);DENNISILLA BAIDOO (b)(6)  
**Subject:** Update on Status of Our Guide

Dear Working Group:

I wanted to send you an update on where we stand as an Editorial Board, and the finalization of our guide.

Last week we received some good news that our target date for completion has been moved out to the end of July, which has given the Editorial Board some extra time to review the comments received from many of you, and the 5 external experts we engaged.

All comments have now been received, and are being reviewed by members of the Editorial Board, especially those who have been key chapter authors. They are working to address all these comments, and over the next 3 weeks the EB will be reviewing the final document one last time, and holding final review meetings. Our current timelines are to have our final meeting on July 12<sup>th</sup>, and a final document to be complete soon after that.

While still undergoing review and update I will say that the document is looking very good: the flow has been much improved, and all sections have been tied together well. The comments from our external experts have been VERY positive, both in terms of the quality of the document, and in their belief it will be of much use and interest to our target audience.

I also wanted to follow up on another issue: you will recall that we had some discussion on how to address information sharing, an issue raised by several WG members. We had a productive meeting on this 3 weeks ago, with active participation from many of you. In the end, we reached consensus that while we agree that this particular issue was not addressed by this WG that it would be best to acknowledge that this work will occur, and that it will likely fall to a future WG. We collected some key thoughts on the issue, and have put them together and will work with CIOMS to consider a symposium or other forum on the subject to move it forward. (b)(4)

this in our Guide itself, as it would not fit with the flow of what is now a very good document focused on AVSS.

As we get closer to a final document, we will stay in touch, and will of course circulate the final version as it goes to the printer.

On behalf of the entire Editorial Board, thank you all for your hard work over the past 3 years, and esp. your recent review and comments of our near final guide.

Regards,

Steven.

**From:** Bailey, Steven R.  
**Sent:** Tue, 8 Dec 2015 22:22:59 +0000  
**To:** Wivel, Ashley E.;Corinne.Jouquelet-Royer@sanofipasteur.com;Destefano, Frank (CDC/OID/NCEZID);Winiecki, Scott (FDA/CBER);holmk@cioms.ch;novilia@biofarma.co.id;(b)(6);Irina.Caplanusi@ema.europa.eu;(b)(6);dongduo@cdr.gov.cn;maurec@who.int;Rmenezes@bio.fiocruz.br;sergio.de.andrade.nishioka@gmail.com;Paulo.santos@bio.fiocruz.br;Harry.A.Seifert@gsk.com;sjolinforbergg@cioms.ch;(b)(6) Zuber, Patrick (CDC who.int)  
**Cc:** Maroko, Robert;dongduo@cdr-adr.org.cn;董铎  
**Subject:** RE: Some Meeting Follow Up  
**Attachments:** CIOMS Manual on Vaccine Active Safety Surveillance All Comments Combined.docx

All (and esp. section owners):

I have combined all of the comments received to date into one document. (we have comments from Frank, Scott, Ashley, Steven, Mimi, Duo Dong, and Corinne). This combined document (it pulls together all the track changes and comments together in one place, which may make your updating of your chapters easier if you have done that already. And, if we all use this version, it may be a bit easier to put it all together when we are done. If everyone sticks to their chapters that they own, and address all the comments/changes, we can then merge the three documents together easily.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

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**From:** Wivel, Ashley E. [mailto:(b)(6):(b)(4)]  
**Sent:** Sunday, November 29, 2015 11:28 PM  
**To:** Bailey, Steven R.; Corinne.Jouquelet-Royer@sanofipasteur.com; fxd1@cdc.gov; Scott.Winiecki@fda.hhs.gov; holmk@cioms.ch; novilia@biofarma.co.id;(b)(6);Irina.Caplanusi@ema.europa.eu;(b)(6);dongduo@cdr.gov.cn; maurec@who.int; Rmenezes@bio.fiocruz.br;(b)(6);Paulo.santos@bio.fiocruz.br; Harry.A.Seifert@gsk.com; sjolinforbergg@cioms.ch;(b)(6); zuberp@who.int  
**Cc:** Maroko, Robert; dongduo@cdr-adr.org.cn; 董铎  
**Subject:** RE: Some Meeting Follow Up

Hi Steven

Thanks very much for the opportunity to review—I added few comments on the chapters for consideration by the chapter authors



Best regards,  
Ashley

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**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** Wednesday, November 18, 2015 9:26 AM  
**To:** Wivel, Ashley E.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);  
[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6)  
[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int);  
[Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6) [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br);  
(b)(6) [sjolin@cioms.ch](mailto:sjolin@cioms.ch); (b)(6) [zuber@who.int](mailto:zuber@who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎  
**Subject:** RE: Some Meeting Follow Up

Thanks Ashley. Actually this raises a good point: if anyone else is still planning on providing comments, could you let us all know when you plan on doing so. I think all the chapter owners would appreciate knowing when to expect the last comments, so they can efficiently update.

If anyone is still planning on sending comments on the completed section, please let us all know, and include when you will provide comments (and upon which version).

Many thanks,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Wivel, Ashley E. [<mailto:ashley.wivel@merck.com>]  
**Sent:** Wednesday, November 18, 2015 9:21 AM  
**To:** Bailey, Steven R.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);  
[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6); (b)(4)  
[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); (b)(4); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int);  
[Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6) [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br);  
(b)(6); (b)(4); [sjolin@cioms.ch](mailto:sjolin@cioms.ch); (b)(6); (b)(4) [zuber@who.int](mailto:zuber@who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎  
**Subject:** RE: Some Meeting Follow Up

Hi Steven

Thanks very much for keeping us on track and helping to coordinate the complex project. I plan to review the last version of the chapters (with comments from srb, skw, cjr) which was sent around recently and to add my comments by Monday 23 November at the latest(hopefully sooner!)

I will loop back with you and Rob separately to discuss the introduction

Best regards,  
Ashley

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**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** Tuesday, November 17, 2015 5:43 PM  
**To:** [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [k; dongduo@cdr.gov.cn](mailto:k; dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforbergg@cioms.ch](mailto:sjolinforbergg@cioms.ch); (b)(6); [zuberp@who.int](mailto:zuberp@who.int)  
**Cc:** Wivel, Ashley E.; Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); Bailey, Steven R.; 董铎  
**Subject:** RE: Some Meeting Follow Up

All:

Just taking a status check to see where everything stands, and everyone's preferred next steps. I think we will need to adjust our business plan a bit (which is fine, we will still be ready for Ghana)

Here is current status of each item:

- 1) Thorough review of Latest Draft of All Chapters: Largely Complete: comments received from Corinne, Duo Dong, Steven, Frank, Scott, Mimi, and, perhaps someone I am missing.
- 2) Chapter 3, Table 3.3, Section 3.4: Novi has provided text to Irina. Awaiting further edits from Irina
- 3) Chapter 3, 3.5/3.6: Done. Scott provided to the entire group
- 4) Introduction: Intro/Algorithm/RACI: Complete and Circulated to Team. Comments Received
- 5) Introduction: Structured Approach: Ashley has completed a draft. Rob Maroko to review (and then I will review)
- 6) Ethical Section: Comments Received along with the comments (item 1 above).

Thanks to everyone who has provided authorship/comments to date. We are making good progress. If my summary above is up to date, the following are our next steps:

- 1) **Steven/Scott/Frank:** Update Chapters 1/2/3 with comments from others. I have not had time to complete this yet. **Frank** and **Scott:** what is the status for Chapter 2 and 3? We had originally said these would be complete by Nov 23<sup>rd</sup>. I will need at least until December 1<sup>st</sup>. Frank/Scott: is this workable for you? If not, simply propose a date and I will re-work our timelines appropriately (and Frank: see item 3 below)
- 2) **Irina:** Awaiting final text for section 3.4 and table 3.3. When do you think that will be ready? Once ready, we can circulate to the larger group.
- 3) **Frank:** once we have text from Irina (item 2), will you be able to incorporate this and the text from Scott for 3.6 into a final version of Chapter 3?
- 4) **Steven/Ashley/Rob:** **Rob:** when will you have reviewed the draft that Ashley provided? When complete, I will review and incorporate into a complete introduction. I will circulate to all at this point. I will aim for December 1<sup>st</sup> for this as well, or whatever date we land on for completion of all chapters.



- 5) **Someone (Volunteer Please)**: The ethical section needs to be re-worked with all the comments received. While this currently sits in Chapter 3, but not sure it belongs there. It was not originally authored by Frank, and he has so much on his plate, that it would be helpful if someone else would take on the rework of this section (and leading a discussion of where it best belongs).

Once I hear from everyone (and especially those **bolded** with todo items, including myself), I will re-work our business plan and dates for next steps. Ideally we will get everything roughly into the same timelines (Intro/Chapters 1-3/Additional Chapter 3 material/Ethical Section) probably by December 15<sup>th</sup> (earlier if everyone agrees, but hopefully before Christmas). If we can do this, then we will be able to relax over the holiday season, and we can circulate everything in the new year for one last look to our group and get this to everyone at least a month ahead of the meeting in Ghana.

Regards, and thanks,

Steven.

All:

We are just 1 week away from our first set of deadlines for TG2 (November 1<sup>st</sup> if a week from this Sunday), and I want to make sure we were moving along, and either encourage everyone to provide updates, or, if necessary, rework our deliverable date.

From our business plan, here is what is due by November 1<sup>st</sup>:

- Thorough review of Chapters 1, 2 and 3, with track changes/comments to Chapter owners **(ALL)**
- Chapter 3: Table 3.3, Section 3.4: Update/Write: **(Novi/Irina)**
- Chapter 3: Sections 3.5 and 3.6: Update/Write: **(Scott)**
- Introduction: Update/Write section 1 (intro), section 2 (algorithm), section 3 (RACI): **(Steven)**
- Introduction: Write Section 4 (structure approach to reviewing data) **(Ashley/Rob (draft 1))**
- Ethical Section (end of chapter 3 now): Carefull Review/update: **(ALL)**

Per previous e-mail, I have already completed bullet 4 and circulated. I am now providing my thorough review of the first 3 chapters, with special attention to the ethical section (see attached).

Hoping this encourages everyone to move forward with the above. However, I do understand how busy schedules are, so let's see how everyone does over the coming week, and we can consider moving our deadlines as needed. Also, based on where we are, I would like to set up a telecon of the group in mid November or so to go over any open items or issues.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA

Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Bailey, Steven R.

**Sent:** Monday, October 12, 2015 12:58 PM

**To:** Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bergman, Ulf (b)(6); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi (b)(6); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Nishioka, Sergio (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sjolín\_Forsberg Gunilla; Tebaa, Amina (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert; 'dongduo@cdr-adr.org.cn'

**Subject:** RE: Some Meeting Follow Up

**Importance:** High

All:

Hope everyone is well. I wanted to make sure we were still keeping up the momentum for TG2. So I have gone ahead and completed one of my deliverables for the project. Please find attached a DRAFT of an update to the Introduction. It includes 3 of the 4 pieces: the opening, the RACI, and the Algorithm.

The last piece of the intro is the (b)(4)

(b)(4)

Ashley and Rob have agreed to take a stab at adding this piece (first draft), and my hope is that by providing this it will be helpful in moving this forward. Ashley/Rob: please reach out if needed as we move this forward.

Please keep in mind the remaining activities per our business plan:

For November 1<sup>st</sup>:

- All to review Chapters 1, 2, and 3 very carefully. Please send your comments to all, and the owner of each section will consolidate those comments and provide the next draft. Please note the revised drafts are due November 23<sup>rd</sup>, so it is very important that you provide your comments by NOVEMBER 1<sup>st</sup>, as discussed. [as a reminder, Chapter Owners are Chapter 1: Steven, Chapter 2: Scott, Chapter 3: Frank]
- Novi/Irina/Scott: Chapter 3 has some sections that still need to be completed, and you all kindly "volunteered" to work on these sections (Table 3.3/section 3.4 (Irina/Novi) and section 3.5/3.6 (Scott))
- All: Review the "ethical section" of chapter 3, with an eye towards how it fits with the rest of the chapter, and any required changes.

I know we committed to tight timelines, but it would be great if we can deliver. If we can work on the 3 bullets above by the 1<sup>st</sup> of November, we really will be in good shape to have all of our deliverables finalized (per our group) before the year-end holidays, and allow review by the larger group before we all meet in Ghana.



If anyone feels a telecon would be helpful at any point in the process (this entire group, or a subset), please let me know and we will work to arrange.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Bailey, Steven R.

**Sent:** Wednesday, September 30, 2015 4:48 PM

**To:** Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bergman, Ulf ((b)(6)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi ((b)(6)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Nishioka, Sergio ((b)(6)); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sjolín\_Forsberg Gunilla; Tebaa, Amina ((b)(6)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert; Bailey, Steven R.

**Subject:** Some Meeting Follow Up

All (Primarily TG 2 members and key stakeholders)

Please find attached some promised documents (sorry for the delay).

Attached are:

- 1) The Updated Business Plan for TG2. Please pay special attention to your assignments and due dates in the business plan. I will send reminders in about 2 weeks to try to keep us on track. Please feel free to offer updates or suggestions if I missed anything.
- 2) Attached is our preliminary RACI. Will require more work as we move forward, but a good start.
- 3) The latest draft of the Introduction that we discussed at the meeting. Ashley, Rob, Scott and others who offered to work on this (including myself), please compare against the business plan for what we agreed to as next steps. If anyone feels a small telecon to further discuss the intro is needed, do not hesitate to request, and I can arrange.

It was a pleasure seeing most of you in Collegeville, and for those who could not attend, look forward to seeing you in Ghana. I will trust everyone will move forward with our work as outlined in the business plan, and will check in in a few weeks. If any questions, please reach out.

Regards,



Steven

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Holm Karin [<mailto:holmkarin@cioms.ch>]

**Sent:** Thursday, September 24, 2015 11:03 AM

**To:** Abdoellah, Siti (alt) (b)(6); Arlett, Peter ([Peter.Arlett@ema.europa.eu](mailto:Peter.Arlett@ema.europa.eu)); Ayoub, Ayman; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Bailey, Steven R.; Benkirane, Raja (b)(6); Bergman, Ulf (b)(6); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)); Bonhoeffer, Jan (alt) ([j.bonhoeffer@brightoncollaboration.org](mailto:j.bonhoeffer@brightoncollaboration.org)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Ceuppens, Marc ([mceuppe1@its.jnj.com](mailto:mceuppe1@its.jnj.com)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mimi (b)(6); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ([alex.dodoo@umcafrica.org](mailto:alex.dodoo@umcafrica.org)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Gregory, William (NYC); Gunale, Bhagwat (alt) ([bhagwat.gunale@seruminstitute.com](mailto:bhagwat.gunale@seruminstitute.com)); HAMID, T. Bahdar Johan (b)(6); Heiles, Bernhard <[bernhard.heiles@merck.com](mailto:bernhard.heiles@merck.com)>; Heininger, Ulrich ([ulrich.heininger@ukbb.ch](mailto:ulrich.heininger@ukbb.ch)); Holm Karin; Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Keller-Stanislawski ([Brigitte.Keller-Stanislawski@pei.de](mailto:Brigitte.Keller-Stanislawski@pei.de)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kulkarni, Prasad ([drpsk@seruminstitute.com](mailto:drpsk@seruminstitute.com)); Kurz, Xavier ([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Lindquist, Marie ([Marie.Lindquist@who-umc.org](mailto:Marie.Lindquist@who-umc.org)); Martin, David ([David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Mentzer, Dirk ([Dirk.Mentzer@pei.de](mailto:Dirk.Mentzer@pei.de)); Nishioka, Sergio (b)(6); Nohynek Anna ([Hanna.Nohynek@thl.fi](mailto:Hanna.Nohynek@thl.fi)); Oberle, Doris (alt2) ([Doris.Oberle@pei.de](mailto:Doris.Oberle@pei.de)); Patel, Mayur (alt) ([PatelMayur@MedImmune.com](mailto:PatelMayur@MedImmune.com)); Ramkishan, Ajmeer (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Shimabukuro, Tom (alt) ([ayv6@cdc.gov9](mailto:ayv6@cdc.gov9)); Sjolín, Forsberg Gunilla; Srivastava, Swati (alt) (b)(6); Tebaa, Amina (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Youssef, Mona (b)(6); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Le\_Roux Susanne; Habersaat, Katrine (DCE-VPI); Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert

**Subject:** Philly meeting group photo

Dear All,

Sending you the group photo from the Philadelphia meeting, which I think reflects on our faces the positive feelings we had about what we achieved at this meeting.

I will also shortly be sending you information about how to access the SharePoint website in an easier manner to get the latest drafts and background documents (I have not yet posted all the updates but shall in coming few weeks).

You will also receive within the coming few weeks, the Philly meeting report so that everyone will feel up-to-date and ready to contribute to this next phase of further writing and editing. Even if you have had little time to involve yourself until now, the Editorial Team can really use your help, expertise, and support to produce a useful guide to Vaccine Safety for new and new-to-you (as we were calling them for short) vaccines.

Please be already planning on attending the next 8<sup>th</sup> meeting to be hosted in Accra, Ghana by the Ghana Food and Drugs Authority, in March or April 2016, as announced by Mimi Darko on the second day of our meeting. We will be sending out a doodle to help determine the best date.

Best regards,  
Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holm@cioms.ch](mailto:holm@cioms.ch)

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**From:** Bailey, Steven R.  
**Sent:** Tue, 6 Sep 2016 16:34:40 +0000  
**To:** Corinne.Jouquelet-Royer@sanofipasteur.com;Zuber, Patrick (CDC who.int);Paulo.santos@bio.fiocruz.br;novilia@biofarma.co.id;Destefano, Frank (CDC/OID/NCEZID);Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu);'Holm Karin'  
**Cc:** Rago Lembit (ragol@cioms.ch);Heininger, Ulrich  
**Subject:** FW: ideas for exec summary  
**Attachments:** EXECUTIVE SUMMARY 08102016.docx

Dear Editorial Board:

As you will recall, we had reviewed an executive summary of our document (authored by Uli, with edits from Patrick, Irina, and myself).

It has been suggested that we submit this summary to Vaccine or another publication as part of the promotion of our full document.

Could you please advise on your thoughts re: who should be listed as authors of this summary, and who you would like to be the corresponding author. My initial thought was to include the entire editorial board, with Uli, and that I could serve as corresponding author for logistics and linking this to our document. But I am open to the consensus of all of you.

Regards,

Steven.

PS: as a status update: our document is basically complete. Unfortunately, with Karin's departure from CIOMS, we are still determining how we will move forward with actually publishing logistics. Now that holidays (and sadly, summer) are over, I will work with Lembit to figure out next steps.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

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**From:** Bailey, Steven R.  
**Sent:** Wed, 30 Sep 2015 20:47:58 +0000  
**To:** Holm Karin;Bachtiar, Novilia (novilia@biofarma.co.id);Bergman, Ulf  
(b)(6);Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu);Darko, Mimi  
(b)(6);Destefano, Frank (CDC/OID/NCEZID);Duo, Dong  
(dongduo@cdr.gov.cn);Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com);Maure,  
Christine (maurec@who.int);Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br);Nishioka, Sergio  
(b)(6);Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br);Seifert, Harry  
(Harry.A.Seifert@gsk.com);Sjolin\_Forsberg Gunilla; (b)(6);Winiecki, Scott  
(FDA/CBER);Zuber, Patrick (CDC who.int)  
**Cc:** Ashley Wivel (ashley.wivel@merck.com);Maroko, Robert;Bailey, Steven R.  
**Subject:** Some Meeting Follow Up  
**Attachments:** TG2 Raci.xls, TG2 Business Plan 09 23 2015.pptx, CIOMS Intro DRAFT 09 23  
2015.docx

All (Primarily TG 2 members and key stakeholders)

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SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** Thursday, September 24, 2015 11:03 AM  
**To:** (b)(6); Arlett, Peter (Peter.Arlett@ema.europa.eu); Ayoub,

Ayman; Bachtiar, Novilia (novilia@biofarma.co.id); Bahri, Priya (Priya.Bahri@ema.europa.eu); Bailey, Steven R.; Benkirane, Raja (b)(6); Bergman, Ulf (b)(6); Blum, Michael (BlumM@MedImmune.com); Bonhoeffer, Jan (alt) (j.bonhoeffer@brightoncollaboration.org); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Ceuppens, Marc (mceuppe1@its.jnj.com); Chandler, Rebecca (alt) (rebecca.chandler@who-umc.org); Darko, Mimi (b)(6); Dawei, Liu (liudw929@126.com); DeStefano, Frank (fxd1@cdc.gov); Dodoo, Alex (alex.dodoo@umcafrica.org); Duo, Dong (dongduo@cdr.gov.cn); Gregory, William (NYC); Gunale, Bhagwat (alt) (bhagwat.gunale@seruminstitute.com); HAMID, T. Bahdar Johan (b)(6); Heiles, Bernhard <bernhard.heiles@merck.com>; Heininger, Ulrich (ulrich.heininger@ukbb.ch); Holm Karin; Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); Keller-Stanislawski (Brigitte.Keller-Stanislawski@pei.de); Kilpi, Terhi (terhi.kilpi@thl.fi); Kulkarni, Prasad (drpsk@seruminstitute.com); Kurz, Xavier (Xavier.Kurz@ema.europa.eu); Lindquist, Marie (Marie.Lindquist@who-umc.org); Martin, David (David.Martin@fda.hhs.gov); Maure, Christine (maurec@who.int); Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br); Mentzer, Dirk (Dirk.Mentzer@pei.de); Nishioka, Sergio (b)(6); Nohynek Anna (Hanna.Nohynek@thl.fi); Oberle, Doris (alt2) (Doris.Oberle@pei.de); Patel, Mayur (alt) (PatelMayur@MedImmune.com); Ramkishan, Ajmeer (b)(6); Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Seifert, Harry (Harry.A.Seifert@gsk.com); Shimabukuro, Tom (alt) (ayv6@cdc.gov9); Sjolín\_Forsberg Gunilla; Srivastava, Swati (alt) (b)(6); Tebaa, Amina (b)(6); Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov); Youssef, Mona (b)(6); Zuber, Patrick (zuberp@who.int)

**Cc:** Le\_Roux Susanne; Habersaat, Katrine (DCE-VPI); Ashley Wivel (ashley.wivel@merck.com); Maroko, Robert

**Subject:** Philly meeting group photo

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Best regards,

Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety  
Publications Coordinator, CIOMS X Meta-Analysis  
Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holmik@cioms.ch](mailto:holmik@cioms.ch)

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	Responsible/Accountable	Consulted	Informed of Decision/Outcome etc
Review of available data	NRA/MOH/EPI	MAH	
Is there a gap	NRA/MOH/EPI	MPvC MAH other regulatory agencies WHO NGO	
Is the gap need to be addressed w/further action (none/study, etc)	NRA/MOH/EPI	MPvC MAH other regulatory agencies WHO NGO	
What is (broadly) the best type of study for this question (PS, AS, CT)	NRA/MOH/EPI	MPvC MAH other regulatory agencies WHO Academia	
If active safety surveillance, which type	NRA/MOH/EPI	MPvC MAH other regulatory agencies WHO NGO Academia	
Who approves the active safety surveillance	NRA/MOH/EPI		MPvC MAH other regulatory agencies WHO NGO
Who determines action based on results	NRA/MOH/EPI		Public MPvC MAH other regulatory agencies WHO NGO Public
For the following, numerous factors should be taken into account in order to determine who is responsible, accountable, etc. These factors include capabilities, level of expertise, nature of question, availability of resources, how vaccine is being sourced, contractual/legal obligation			
Who designs the active safety surveillance			
Who implements the active safety surveillance			
Who pays for the study			
Who interprets the results			
Who disseminates the results	NRA/MOH		
Who owns the data			

**PARTICIPANT LIST****VACCINE SAFETY WG MEETING****PHILADELPHIA 21-22 SEPTEMBER 2015**

?Visa

Ajmeer Ramkishan	Indian Central Drugs Standard Control Organization	(b)(6)
Bernhard Heiles	MERCK (U.S)	bernhard.heiles@merck.com
Christine Maure (alt)	WHO	maurec@who.int
Dong Duo	China Food & Drug Administration	dongduo@cdr.gov.cn
Frank DeStefano	CDC	fxd1@cdc.gov
Harry Seifert	GlaxoSmithKline	Harry.A.Seifert@gsk.com
Irina Caplanusi	European Medicines Agency	Irina.Caplanusi@ema.europa.eu
Karin Holm	CIOMS Technical Coordinator	holm@cioms.ch
Marc Ceuppens (alt)	Crucell/Janssen/Johnson & Johnson	mceuppe1@its.jnj.com
Michael Blum	MedImmune/ AstraZeneca	BlumM@medimmune.com
Mimi Darko Delese (alt)	Ghana Food & Drugs Authority	mimidarko66@yahoo.co.uk
Novilia Sjafri Bachtiar	Bio Farma Indonesia	novilia@biofarma.co.id
Patrick Zuber	WHO	zuberp@who.int
Priya Bahri	European Medicines Agency	priya.bahri@emea.europa.eu
Rebecca Chandler (alt)	WHO	rebecca.chandler@who-umc.org
Scott Winiecki (alt)	US Food & Drug Administration	Scott.Winiecki@fda.hhs.gov
Steven Bailey	Pfizer	Steven.R.Bailey@pfizer.com
Ulf Bergman	CIOMS Senior Adviser	bergmanu@cioms.ch / (b)(6)
<u>Guest participants</u>		
Rob Maroko	Pfizer	Robert.Maroko@pfizer.com
Robb Butler	WHO Denmark	butlerr@who.int



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**From:** Bailey, Steven R.  
**Sent:** Wed, 29 Jun 2016 17:12:06 +0000  
**To:** Corinne.Jouquelet-Royer@sanofipasteur.com; Zuber, Patrick (CDC who.int); Destefano, Frank (CDC/OID/NCEZID); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); 'Holm Karin'; Paulo.santos@bio.fiocruz.br'; Bachtiar, Novilia (novilia@biofarma.co.id)  
**Cc:** Bailey, Steven R.  
**Subject:** Editorial Board: Next Steps

All:

Just wanted to provide a brief summary of the agreed upon next steps, so you can plan your time for review as we enter our last 2 weeks of work. This was agreed upon at our meeting yesterday, but hopefully this will lay it out clearly:

1. Update of the Draft: the document is being updated this week to reflect our meeting results, and the agreements we reached. Karin, Irina and I are making updates as well with some new/re-organized text. We are aiming for Friday.
2. Karin will forward an updated version to the EB once she has had time to organize it: either this Friday or early next week.
3. The expectation is that each member of the Ed Board will review this version, and will provide edits (preferable) or comments via track changes.
  - A. We ask the EB to focus on the few remaining comments, and the new/updated text highlighted throughout in green.
  - B. Given the time, if you want changes to text, please provide the new text. We will not have time to write new text as a group. It will be better to accept or reject track changes
4. Please forward your tracked change document (labeled with your initials, please) to Karin and I by the 10<sup>th</sup> of July. I will need to combine all the tracked changes into one document on the 11<sup>th</sup>, and need some time to do this.
5. We will meet again on July 12<sup>th</sup>. (I will convert the meeting hold to webex). This will hopefully be our final meeting and we will complete all open review items.

Please let me know if you have any questions.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

**From:** Bailey, Steven R.  
**Sent:** Mon, 11 Apr 2016 16:25:17 +0000  
**To:** Holm Karin;Bachtiar, Novilia (novilia@biofarma.co.id);Bahri, Priya (Priya.Bahri@ema.europa.eu);Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu);Darko, Mimi (b)(6);Destefano, Frank (CDC/OID/NCEZID);Dodoo, Alex (b)(6);Heininger, Ulrich (ulrich.heininger@ukbb.ch);Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com);Maure, Christine (maurec@who.int);Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br);Straus, Walter (walter\_straus@merck.com);Winiecki, Scott (FDA/CBER);Zuber, Patrick (CDC who.int);Irina.Caplanusi@ema.europa.eu;Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Rantz, Reggie  
**Subject:** RE: CIOMS TC on the Guide -- Thurs. 14 April at 4.00 pm GVA  
**Importance:** High

All:

As we move into the home stretch of our CIOMS project, we have decided to set up a weekly meeting to move these forward as efficiently as possible. This meeting will include the members of the Editorial Board (Novilia, Irina, Frank, Corinne, Paulo, and Patrick) and some very active contributors/authors to the document or critical voices (Karin, Scott, Uli, Priya, Walter, Mimi and Alex). This was discussed at a recent post Ghana debrief, so many of you are already aware of this, but the concept may be new to a few of you.

I am going to ask my assistant to set these meeting up ASAP, but want to check with everyone that we are choosing the best (as opposed to perfect) time.

Per our discussion last week we planned on doing these meeting every Friday, at 9:00 Eastern Time (NY), for 2 hours. Please let me know if you have major objections to this time or plan, and we will see if we can accommodate (understanding you may be booked in the short term, but eventually would be able to make it. If you feel the time must be move, please send an alternative date/time so we can land on something over the next 2-3 days. It might be a matter of simply saying which days of the week you absolutely can't make it on an ongoing basis. Again, I am afraid there will be no perfect time, but we will do our best.

(the basic parameters are: I needs to be between 8:30 and 11 (maybe 12) PM Eastern time so not too early in US or too late Europe). So it is really a matter of which day of the week, and for how long (we could consider just making it 1 hour which is probably enough if we meet weekly.

Regards,

Steven.

PS:

Steven R. Bailey, MD MPH MBA

*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670



**From:** Bailey, Steven R.  
**Sent:** Thu, 14 Jan 2016 15:54:29 +0000  
**To:** Caplanusi Irina;Destefano, Frank (CDC/OID/NCEZID);MAURE, Christine;Wivel, Ashley E.;Corinne.Jouquelet-Royer@sanofipasteur.com;Winiecki, Scott (FDA/CBER);holmk@cioms.ch;novilia@biofarma.co.id (b)(6) (b)(6) o.co.uk;dongduo@cdr.gov.cn;Rmenezes@bio.fiocruz.br; (h)(6) Paulo.santos@bio.fiocruz.br;Harry.A.Seifert@gsk.com;sjolinforsbergg@cioms.ch (h)(6);Zuber, Patrick (CDC who.int);Maroko, Robert;董铎  
**Cc:** Rantz, Reggie;Straus, Walter L.  
**Subject:** CIOMS TG1 Final Draft Review  
**Attachments:** TG1 Intro and Chapters 1-3.docx

All:

In preparation for our telecon and webex scheduled for February 4<sup>th</sup>, I am attaching a consolidated version of all our work to date. The attached document contains the overall document introduction, and then Chapters 1, 2 and 3. The prime authors of each chapter have consolidated and responded to all comments received to date. Any comments remaining are those that still need to be addressed by this group at our meeting (e.g., comments where there is not alignment across all the group).

A few other notes:

- 1) There is quite a bit of new text that has not been seen by the larger group yet:
  - a. The introduction will be new to those that did not work on it
  - b. Table 3.4 and accompanying text which was updated by Novi and Irina (numbering changed since they updated)
  - c. Section 3.5 which was updated by Scott (numbering changed since he wrote it)
  - d. Section 3.7, the ethical aspects, updated by Christine.

I have highlighted all of these new section in GREEN TEXT and you may wish to pay extra attention to these section and consider sending comments on them TO THE AUTHOR of that section and copy the group. We will have to come up a with a process for update this new master document appropriately.

- 2) There appears to have been some loss of version control along the way, and there is now some overlap and difference in text between sections 3.4 and 3.5. Could I request Frank (probably with Scott) take a look at these two sections, and determine how they should be best consolidated. I am not sure what happened, and perhaps I simply confused the various versions that had been sent to me for consolidation.

I will be travelling extensively between now and the 4<sup>th</sup>, so it is unlikely I will be able to do further work on this document. This should be the version we will use for our discussion. At that meeting we can discuss any additional changes and comments that you may have and how these can be incorporated. Also, given I will not be able to attend the meeting in Ghana, we will need to discuss who will take over the next drafts of this master document.

Kind regards,

Steven.

Chapter Authors: (Scott, Frank and I) please be prepared to walk through all open questions on your sections, and raise any issues/questions you need in order to have sections finalized before Ghana.

Many thanks,

Steven.

~~~~~  
~~~~~

**\*Steven to host\***

-- Do not delete or change any of the following text. --

Meeting Information

CLICK TO JOIN:

<https://collaborate.webex.com/collaborate/j.php?MTID=m5912e80d004ec6d98739e8dd2bd66d2d>

No internet or data connection?

JOIN BY PHONE

(b)(6)

Call-in toll-free number (US/Canada)

Call-in toll number (US/Canada)

Access code:

(b)(6)

Global call-in numbers:

<https://collaborate.webex.com/collaborate/globalcallin.php?serviceType=MC&ED=404436902&tollFree=1>

Toll-free dialing restrictions:

[http://www.webex.com/pdf/tollfree\\_restrictions.pdf](http://www.webex.com/pdf/tollfree_restrictions.pdf)

WebEx Meeting and Support Details

Meeting number:

(b)(6)

Meeting password:

Host key:

(b)(6)

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. You should inform all meeting attendees prior to recording if you intend to record the meeting.

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**From:** Bailey, Steven R.  
**Sent:** Tue, 28 Jun 2016 16:15:52 +0000  
**To:** Holm Karin; Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: missing references

Karin:

(b)(4)

S.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holm@cioms.ch]  
**Sent:** Tuesday, June 28, 2016 12:00 PM  
**To:** Bailey, Steven R.; DeStefano, Frank (fxd1@cdc.gov)  
**Subject:** missing references

Steven and Frank,

I cannot find the references to this even if I go back to Feb 2015. I think it was copied from another document so there were never any actual references behind it.

#### 3.3.1.1. Cohort studies

....There are several automated databases available for pharmacoepidemiologic studies (Ref 12<sup>1518</sup>).

So I wonder if this reference I found, would be okay in its place?

#### Automated databases

The identification of large numbers of patients for cohort studies could be facilitated if data can be derived from large automated databases. There are several automated databases available for pharmacoepidemiological studies.<sup>27</sup>

<sup>27</sup> Strom, B. L. (2012) Overview of Automated Databases in Pharmacoepidemiology, in Pharmacoepidemiology, Fifth Edition (eds B. L. Strom, S. E. Kimmel and S. Hennessy), Wiley-Blackwell, Oxford, UK.

<http://onlinelibrary.wiley.com/doi/10.1002/9781119959946.ch11/summary>

**Karin**

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holmkr@cioms.ch](mailto:holmkr@cioms.ch)

*(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)*

**From:** Bailey, Steven R.  
**Sent:** Tue, 5 Jan 2016 22:17:53 +0000  
**To:** Caplanusi Irina; Destefano, Frank (CDC/OID/NCEZID); MAURE, Christine; Wivel, Ashley E.; Corinne.Jouquelet-Royer@sanofipasteur.com; Winiecki, Scott (FDA/CBER); holmk@cioms.ch; novilia@biofarma.co.id; (b)(6); (b)(6); (b)(6); dongduo@cdr.gov.cn; Rmenezes@bio.fiocruz.br; sergio.de.andrade.nishioka@gmail.com; Paulo.santos@bio.fiocruz.br; Harry.A.Seifert@gsk.com; sjolinforsbergg@cioms.ch; (b)(6); Zuber, Patrick (CDC who.int)  
**Cc:** Maroko, Robert; 董铎; Rantz, Reggie; Bailey, Steven R.  
**Subject:** RE: Some Meeting Follow Up  
**Importance:** High

All:

After reviewing all the responses, the only day that will work is Feb 4<sup>th</sup>. By way of this message, can I ask everyone who can to block their calendars for Feb 4<sup>th</sup>, 9 to 11:00 AM, Eastern Standard Time.

**Reggie:**

Could you please set up a Webex/Telecon for those on this mail on February 4<sup>th</sup>, 9-11.

Chapter Authors: Scott, Frank and I: please be prepared to walk through all open questions on your sections, and raise any issues/questions you need in order to have sections finalized before Ghana.

Many thanks,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Bailey, Steven R.  
**Sent:** Monday, December 21, 2015 11:10 AM  
**To:** Caplanusi Irina; Destefano, Frank (CDC/OID/NCEZID); MAURE, Christine; Wivel, Ashley E.; Corinne.Jouquelet-Royer@sanofipasteur.com; Winiecki, Scott (FDA/CBER); holmk@cioms.ch; novilia@biofarma.co.id; ulfkabergman@hotmail.com; (b)(6); dongduo@cdr.gov.cn; Rmenezes@bio.fiocruz.br; (b)(6); Paulo.santos@bio.fiocruz.br; Harry.A.Seifert@gsk.com; sjolinforsbergg@cioms.ch; (b)(6); Zuber, Patrick (CDC who.int)  
**Cc:** Maroko, Robert; 董铎; Bailey, Steven R.; Rantz, Reggie  
**Subject:** RE: Some Meeting Follow Up  
**Importance:** High

Dear All:

We would like to go ahead and start to schedule a telecon/web for February, before calendars fill up. Could you please respond as soon as you can to the proposed times below, and we will schedule where the most people are available. Of course, we will need to prioritize the attendance of the chapter leads (Scott, Frank and I) but will attempt to find a time where almost all are available. Frank/Scott: could you please make sure to respond yourselves as a priority. While we might use the full 2 hour times, I will schedule for this just in case. All times are Eastern Standard Time (New York, US). Apologies to those in Asia as I simply can't to early or late night times in the US.

Feb 1<sup>st</sup>: 9-11

Feb 4<sup>th</sup>: 9-11

Feb 12<sup>th</sup>: 9-11

Feb 16<sup>th</sup>: 9-11

Feb 17<sup>th</sup>: 9-11

Feb 18<sup>th</sup>: 9-11

Feb 19<sup>th</sup>: 9-11

Feb 22<sup>nd</sup>: 9-11

Please respond when you can. I understand it is the holidays, so we will wait until January 6<sup>th</sup> to schedule the meeting.

Kind regards,

Steven

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Caplanusi Irina [<mailto:Irina.Caplanusi@ema.europa.eu>]

**Sent:** Friday, December 18, 2015 11:12 AM

**To:** Bailey, Steven R.; Destefano, Frank (CDC/OID/NCEZID); MAURE, Christine; Wivel, Ashley E.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); Winiecki, Scott (FDA/CBER); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6) [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolin@forsbergg@cioms.ch](mailto:sjolin@forsbergg@cioms.ch); (b)(6) Zuber, Patrick (CDC who.int)

**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎

**Subject:** RE: Some Meeting Follow Up

Dear Steven,

Please find enclosed the draft table 3.3 and section 3.4.

Looking forward to the TC in February and until then I wish you a very happy winter break and holiday season!



Kind regards,  
Irina

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** 16 December 2015 21:21  
**To:** Destefano, Frank (CDC/OID/NCEZID); MAURE, Christine; Wivel, Ashley E.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); Winiecki, Scott (FDA/CBER); [holmik@cioms.ch](mailto:holmik@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6); Caplanusi Irina; [mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforbergg@cioms.ch](mailto:sjolinforbergg@cioms.ch); (b)(6); Zuber, Patrick (CDC who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎  
**Subject:** RE: Some Meeting Follow Up

Thanks Frank. I will load these into a "master" document once we get chapter 2 (no pressure Scott). Then will re-circulate to the larger group.

Consensus (based on a few responses) is that we will aim for a telecon in February (early) timeframe and resolve open issues.

A pleasant holiday and new year to all!

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Wednesday, December 16, 2015 4:13 PM  
**To:** MAURE, Christine; Bailey, Steven R.; Wivel, Ashley E.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); Winiecki, Scott (FDA/CBER); [holmik@cioms.ch](mailto:holmik@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); (b)(6); [sjolinforbergg@cioms.ch](mailto:sjolinforbergg@cioms.ch); (b)(6); Zuber, Patrick (CDC who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎; Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: Some Meeting Follow Up

This revised draft contains a cleaned up version of Chapter 3 taking into consideration suggested edits and comments received to date. (No changes have been made to the other chapters.)

Thanks to all who provided input,  
Frank

Frank DeStefano, MD, MPH



---

**From:** MAURE, Christine [<mailto:maurec@who.int>]  
**Sent:** Wednesday, December 16, 2015 9:45 AM  
**To:** Bailey, Steven R. <[Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com)>; Wivel, Ashley E. <[ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)>;  
[Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); Destefano, Frank (CDC/OID/NCEZID) <[fxd1@cdc.gov](mailto:fxd1@cdc.gov)>;  
Winiecki, Scott (FDA/CBER) <[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)>; [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id);  
(b)(6); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6)  
[dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6)  
[Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolin@cioms.ch](mailto:sjolin@cioms.ch); [atebaa@yahoo.fr](mailto:atebaa@yahoo.fr);  
Zuber, Patrick (CDC who.int) <[zuberp@who.int](mailto:zuberp@who.int)>  
**Cc:** Maroko, Robert <[Robert.Maroko@pfizer.com](mailto:Robert.Maroko@pfizer.com)>; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎 <[dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn)>  
**Subject:** RE: Some Meeting Follow Up

Many thanks Steve

Please find attached the revised ethical section and comments on the other sections.

I would in favour of having a TC prior the meeting in Ghana.

With kind regards  
Christine

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** 15 December 2015 17:20  
**To:** Wivel, Ashley E.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);  
[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6)  
[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6) [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); MAURE, Christine;  
[Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6) [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br);  
[Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolin@cioms.ch](mailto:sjolin@cioms.ch); (b)(6); ZUBER, Patrick Louis F.  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎; Bailey, Steven R.  
**Subject:** RE: Some Meeting Follow Up  
**Importance:** High

All:

In follow up to the below, please find attached a version of our section with an update to Chapter 1. I have gone through the chapter, and made the suggested edits (and dealt with conflicting edits), as well as addressing all comments. The result is a "near final" draft that would be ready for review by the larger CIOMS group when we have all sections updated.

(b)(4)

If I can, I would suggest the other section authors do the same. Once we have collected all of the sections, we can put them into one document, and all the open questions for team discussion will be in

one place. We can then either a) meet ahead of Ghana by telecon to resolve them or b) wait for discussion at Ghana.

My preference would be to try to schedule a telecon in February if the team agrees. That way we can have these items resolved ahead of the next meeting, and make that more productive.

Please let me know your preferences, and I will update our business plan appropriately.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Bailey, Steven R.  
**Sent:** Tuesday, December 8, 2015 5:23 PM  
**To:** 'Wivel, Ashley E.'; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);  
[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holmck@cioms.ch](mailto:holmck@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6)  
[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6) [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int);  
[Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6) [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br);  
[Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforbergg@cioms.ch](mailto:sjolinforbergg@cioms.ch); (b)(6) [zuberp@who.int](mailto:zuberp@who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎  
**Subject:** RE: Some Meeting Follow Up

All (and esp. section owners):

I have combined all of the comments received to date into one document. (we have comments from Frank, Scott, Ashley, Steven, Mimi, Duo Dong, and Corinne). This combined document (it pulls together all the track changes and comments together in one place, which may make your updating of your chapters easier if you have done that already. And, if we all use this version, it may be a bit easier to put it all together when we are done. If everyone sticks to their chapters that they own, and address all the comments/changes, we can then merge the three documents together easily.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670



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**From:** Wivel, Ashley E. [<mailto:ashley.wivel@merck.com>]  
**Sent:** Sunday, November 29, 2015 11:28 PM  
**To:** Bailey, Steven R.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);  
[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holmk@cioms.ch](mailto:holmk@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6)  
[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int);  
[Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br);  
[Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforsbergg@cioms.ch](mailto:sjolinforsbergg@cioms.ch); (b)(6); [zuberp@who.int](mailto:zuberp@who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎  
**Subject:** RE: Some Meeting Follow Up

Hi Steven

Thanks very much for the opportunity to review—I added few comments on the chapters for consideration by the chapter authors

Best regards,  
Ashley

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** Wednesday, November 18, 2015 9:26 AM  
**To:** Wivel, Ashley E.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);  
[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holmk@cioms.ch](mailto:holmk@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6)  
[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int);  
[Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br);  
[Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforsbergg@cioms.ch](mailto:sjolinforsbergg@cioms.ch); (b)(6); [zuberp@who.int](mailto:zuberp@who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎  
**Subject:** RE: Some Meeting Follow Up

Thanks Ashley. Actually this raises a good point: if anyone else is still planning on providing comments, could you let us all know when you plan on doing so. I think all the chapter owners would appreciate knowing when to expect the last comments, so they can efficiently update.

If anyone is still planning on sending comments on the completed section, please let us all know, and include when you will provide comments (and upon which version).

Many thanks,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Wivel, Ashley E. [<mailto:ashley.wivel@merck.com>]  
**Sent:** Wednesday, November 18, 2015 9:21 AM

**To:** Bailey, Steven R.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforbergg@cioms.ch](mailto:sjolinforbergg@cioms.ch); (b)(6); [zuberp@who.int](mailto:zuberp@who.int)  
**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎  
**Subject:** RE: Some Meeting Follow Up

Hi Steven

Thanks very much for keeping us on track and helping to coordinate the complex project. I plan to review the last version of the chapters (with comments from srb, skw, cjr) which was sent around recently and to add my comments by Monday 23 November at the latest(hopefully sooner!)

I will loop back with you and Rob separately to discuss the introduction

Best regards,  
Ashley

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**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** Tuesday, November 17, 2015 5:43 PM  
**To:** [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforbergg@cioms.ch](mailto:sjolinforbergg@cioms.ch); (b)(6); [zuberp@who.int](mailto:zuberp@who.int)  
**Cc:** Wivel, Ashley E.; Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); Bailey, Steven R.; 董铎  
**Subject:** RE: Some Meeting Follow Up

All:

Just taking a status check to see where everything stands, and everyone's preferred next steps. I think we will need to adjust our business plan a bit (which is fine, we will still be ready for Ghana)

Here is current status of each item:

- 1) Thorough review of Latest Draft of All Chapters: Largely Complete: comments received from Corinne, Duo Dong, Steven, Frank, Scott, Mimi, and, perhaps someone I am missing.
- 2) Chapter 3, Table 3.3, Section 3.4: Novi has provided text to Irina. Awaiting further edits from Irina
- 3) Chapter 3, 3.5/3.6: Done. Scott provided to the entire group
- 4) Introduction: Intro/Algorithm/RACI: Complete and Circulated to Team. Comments Received
- 5) Introduction: Structured Approach: Ashley has completed a draft. Rob Maroko to review (and then I will review)
- 6) Ethical Section: Comments Received along with the comments (item 1 above).

Thanks to everyone who has provided authorship/comments to date. We are making good progress. If my summary above is up to date, the following are our next steps:



- 1) **Steven/Scott/Frank:** Update Chapters 1/2/3 with comments from others. I have not had time to complete this yet. **Frank and Scott:** what is the status for Chapter 2 and 3? We had originally said these would be complete by Nov 23<sup>rd</sup>. I will need at least until December 1<sup>st</sup>. Frank/Scott: is this workable for you? If not, simply propose a date and I will re-work our timelines appropriately (and Frank: see item 3 below)
- 2) **Irina:** Awaiting final text for section 3.4 and table 3.3. When do you think that will be ready? Once ready, we can circulate to the larger group.
- 3) **Frank:** once we have text from Irina (item 2), will you be able to incorporate this and the text from Scott for 3.6 into a final version of Chapter 3?
- 4) **Steven/Ashley/Rob: Rob:** when will you have reviewed the draft that Ashley provided? When complete, I will review and incorporate into a complete introduction. I will circulate to all at this point. I will aim for December 1<sup>st</sup> for this as well, or whatever date we land on for completion of all chapters.
- 5) **Someone (Volunteer Please):** The ethical section needs to be re-worked with all the comments received. While this currently sits in Chapter 3, but not sure it belongs there. It was not originally authored by Frank, and he has so much on his plate, that it would be helpful if someone else would take on the rework of this section (and leading a discussion of where it best belongs).

Once I hear from everyone (and especially those **bolded** with todo items, including myself), I will re-work our business plan and dates for next steps. Ideally we will get everything roughly into the same timelines (Intro/Chapters 1-3/Additional Chapter 3 material/Ethical Section) probably by December 15<sup>th</sup> (earlier if everyone agrees, but hopefully before Christmas). If we can do this, then we will be able to relax over the holiday season, and we can circulate everything in the new year for one last look to our group and get this to everyone at least a month ahead of the meeting in Ghana.

Regards, and thanks,

Steven.

All:

We are just 1 week away from our first set of deadlines for TG2 (November 1<sup>st</sup> if a week from this Sunday), and I want to make sure we were moving along, and either encourage everyone to provide updates, or, if necessary, rework our deliverable date.

From our business plan, here is what is due by November 1<sup>st</sup>:

- Thorough review of Chapters 1, 2 and 3, with track changes/comments to Chapter owners **(ALL)**
- Chapter 3: Table 3.3, Section 3.4: Update/Write: **(Novi/Irina)**
- Chapter 3: Sections 3.5 and 3.6: Update/Write: **(Scott)**
- Introduction: Update/Write section 1 (intro), section 2 (algorithm), section 3 (RACI): **(Steven)**
- Introduction: Write Section 4 (structure approach to reviewing data) **(Ashley/Rob (draft 1))**
- Ethical Section (end of chapter 3 now): Carefull Review/update: **(ALL)**

Per previous e-mail, I have already completed bullet 4 and circulated. I am now providing my thorough review of the first 3 chapters, with special attention to the ethical section (see attached).

Hoping this encourages everyone to move forward with the above. However, I do understand how busy schedules are, so let's see how everyone does over the coming week, and we can consider moving our deadlines as needed. Also, based on where we are, I would like to set up a telecon of the group in mid November or so to go over any open items or issues.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Bailey, Steven R.

**Sent:** Monday, October 12, 2015 12:58 PM

**To:** Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bergman, U [REDACTED] (b)(6)  
Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi [REDACTED] (b)(6)  
DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Jouquelet-Royer, Corinne  
([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo  
de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Nishioka, Sergio [REDACTED] (b)(6) Santos, Paulo  
(alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sjolín-Forsberg Gunilla;  
Tebaa, Amina [REDACTED] (b)(6) Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick  
([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert; 'dongduo@cdr-adr.org.cn'

**Subject:** RE: Some Meeting Follow Up

**Importance:** High

All:

Hope everyone is well. I wanted to make sure we were still keeping up the momentum for TG2. So I have gone ahead and completed one of my deliverables for the project. Please find attached a DRAFT of an update to the Introduction. It includes 3 of the 4 pieces: the opening, the RACI, and the Algorithm.

The last piece of the intro is the [REDACTED] (b)(4)

[REDACTED] (b)(4)

Ashley and Rob have agreed to take a stab at adding this piece (first draft), and my hope is that by providing this it will be helpful in moving this forward. Ashley/Rob: please reach out if needed as we move this forward.

Please keep in mind the remaining activities per our business plan:

For November 1<sup>st</sup>:

- All to review Chapters 1, 2, and 3 very carefully. Please send your comments to all, and the owner of each section will consolidate those comments and provide the next draft.



Please note the revised drafts are due November 23<sup>rd</sup>, so it is very important that you provide your comments by NOVEMBER 1<sup>st</sup>, as discussed. [as a reminder, Chapter Owners are Chapter 1: Steven, Chapter 2: Scott, Chapter 3: Frank]

- Novi/Irina/Scott: Chapter 3 has some sections that still need to be completed, and you all kindly “volunteered” to work on these sections (Table 3.3/section 3.4 (Irina/Novi) and section 3.5/3.6 (Scott))
- All: Review the “ethical section” of chapter 3, with an eye towards how it fits with the rest of the chapter, and any required changes.

I know we committed to tight timelines, but it would be great if we can deliver. If we can work on the 3 bullets above by the 1<sup>st</sup> of November, we really will be in good shape to have all of our deliverable finalized (per our group) before the year-end holidays, and allow review by the larger group before we all meet in Ghana.

If anyone feels a telecon would be helpful at any point in the process (this entire group, or a subset), please let me know and we will work to arrange.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Bailey, Steven R.

**Sent:** Wednesday, September 30, 2015 4:48 PM

**To:** Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bergman, Ulf (b)(6); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi (b)(6); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Nishioka, Sergio (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sjolín\_Forsberg Gunilla; Tebaa, Amina (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert; Bailey, Steven R.

**Subject:** Some Meeting Follow Up

All (Primarily TG 2 members and key stakeholders)

Please find attached some promised documents (sorry for the delay).

Attached are:

- 1) The Updated Business Plan for TG2. Please pay special attention to your assignments and due dates in the business plan I will send reminders in about 2 weeks to try to keep us on track. Please feel free to offer updates or suggestions if I missed anything
- 2) Attached is our preliminary RACI. Will require more work as we move forward, but a good start.
- 3) The latest draft of the Introduction that we discussed at the meeting. Ashley, Rob, Scott and others who offered to work on this (including myself), please compare against the business plan for what we agreed to as next steps. If anyone feels a small telecon to further discuss the intro is needed, do not hesitate to request, and I can arrange.

It was a pleasure seeing most of you in Collegeville, and for those who could not attend, look forward to seeing you in Ghana. I will trust everyone will move forward with our work as outlined in the business plan, and will check in in a few weeks. If any questions, please reach out.

Regards,

Steven

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Holm Karin [<mailto:holmkarin@cioms.ch>]

**Sent:** Thursday, September 24, 2015 11:03 AM

**To:** Abdoellah, Siti (alt) (b)(6); Arlett, Peter ([Peter.Arlett@ema.europa.eu](mailto:Peter.Arlett@ema.europa.eu)); Ayoub, Ayman; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Bailey, Steven R.; Benkirane, Raja (b)(6); Bergman, Ulf (b)(6); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)); Bonhoeffer, Jan (alt) ([j.bonhoeffer@brightoncollaboration.org](mailto:j.bonhoeffer@brightoncollaboration.org)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Ceuppens, Marc ([mceuppe1@its.inj.com](mailto:mceuppe1@its.inj.com)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mimi (b)(6); Dawei, Liu (b)(6); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ([alex.dodoo@umcafrica.org](mailto:alex.dodoo@umcafrica.org)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Gregory, William (NYC); Gunale, Bhagwat (alt) ([bhagwat.gunale@seruminstitute.com](mailto:bhagwat.gunale@seruminstitute.com)); HAMID, T. Bahdar Johan (b)(6); Heiles, Bernhard <[bernhard.heiles@merck.com](mailto:bernhard.heiles@merck.com)>; Heininger, Ulrich ([ulrich.heininger@ukbb.ch](mailto:ulrich.heininger@ukbb.ch)); Holm Karin; Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Keller-Stanislawski ([Brigitte.Keller-Stanislawski@pei.de](mailto:Brigitte.Keller-Stanislawski@pei.de)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kulkarni, Prasad ([drpsk@seruminstitute.com](mailto:drpsk@seruminstitute.com)); Kurz, Xavier ([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Lindquist, Marie ([Marie.Lindquist@who-umc.org](mailto:Marie.Lindquist@who-umc.org)); Martin, David ([David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Mentzer, Dirk ([Dirk.Mentzer@pei.de](mailto:Dirk.Mentzer@pei.de)); Nishioka, Sergio (b)(6); Nohynek Anna ([Hanna.Nohynek@thl.fi](mailto:Hanna.Nohynek@thl.fi)); Oberle, Doris (alt2) ([Doris.Oberle@pei.de](mailto:Doris.Oberle@pei.de)); Patel, Mayur (alt) ([PatelMayur@MedImmune.com](mailto:PatelMayur@MedImmune.com)); Ramkishan, Ajmeer (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Shimabukuro, Tom (alt) ([ayv6@cdc.gov](mailto:ayv6@cdc.gov)); Siolin Forsberg Gunilla; Srivastava, Swati (alt) (b)(6); Tebaa, Amina (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Youssef, Mona (b)(6); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Le\_Roux Susanne; Habersaat, Katrine (DCE-VPI); Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko,



Robert

**Subject:** Philly meeting group photo

Dear All,

Sending you the group photo from the Philadelphia meeting, which I think reflects on our faces the positive feelings we had about what we achieved at this meeting.

I will also shortly be sending you information about how to access the SharePoint website in an easier manner to get the latest drafts and background documents (I have not yet posted all the updates but shall in coming few weeks).

You will also receive within the coming few weeks, the Philly meeting report so that everyone will feel up-to-date and ready to contribute to this next phase of further writing and editing. Even if you have had little time to involve yourself until now, the Editorial Team can really use your help, expertise, and support to produce a useful guide to Vaccine Safety for new and new-to-you (as we were calling them for short) vaccines.

Please be already planning on attending the next 8<sup>th</sup> meeting to be hosted in Accra, Ghana by the Ghana Food and Drugs Authority, in March or April 2016, as announced by Mimi Darko on the second day of our meeting. We will be sending out a doodle to help determine the best date.

Best regards,

Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

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**From:** Bailey, Steven R.  
**Sent:** Mon, 12 Oct 2015 16:57:43 +0000  
**To:** Holm Karin;Bachtiar, Novilia (novilia@biofarma.co.id);Bergman, Ulf  
(b)(6) Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu);Darko, Mimi  
(b)(6) );Destefano, Frank (CDC/OID/NCEZID);Duo, Dong  
(dongduo@cdr.gov.cn);Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com);Maure,  
Christine (maurec@who.int);Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br);Nishioka, Sergio  
(sergio.de.andrade.nishioka@gmail.com);Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br);Seifert, Harry  
(Harry.A.Seifert@gsk.com);Sjolin\_Forsberg Gunilla;Tebaa, Amina (b)(6);Winiecki, Scott  
(FDA/CBER);Zuber, Patrick (CDC who.int)  
**Cc:** Ashley Wivel (ashley.wivel@merck.com);Maroko, Robert;dongduo@cdr-  
adr.org.cn  
**Subject:** RE: Some Meeting Follow Up  
**Attachments:** CIOMS Intro DRAFT SRB V2.docx  
**Importance:** High

All:

Hope everyone is well. I wanted to make sure we were still keeping up the momentum for TG2. So I have gone ahead and completed one of my deliverables for the project. Please find attached a DRAFT of an update to the Introduction. It includes 3 of the 4 pieces: the opening, the RACI, and the Algorithm.

The last piece of the intro is the (b)(4)  
(b)(4) Ashley and Rob have agreed to take a stab at adding this piece (first draft), and my hope is that by providing this it will be helpful in moving this forward. Ashley/Rob: please reach out if needed as we move this forward.

Please keep in mind the remaining activities per our business plan:

For November 1<sup>st</sup>:

- All to review Chapters 1, 2, and 3 very carefully. Please send your comments to all, and the owner of each section will consolidate those comments and provide the next draft. Please note the revised drafts are due November 23<sup>rd</sup>, so it is very important that you provide your comments by NOVEMBER 1<sup>st</sup>, as discussed. [as a reminder, Chapter Owners are Chapter 1: Steven, Chapter 2: Scott, Chapter 3: Frank]
- Novi/Irina/Scott: Chapter 3 has some sections that still need to be completed, and you all kindly "volunteered" to work on these sections (Table 3.3/section 3.4 (Irina/Novi) and section 3.5/3.6 (Scott))
- All: Review the "ethical section" of chapter 3, with an eye towards how it fits with the rest of the chapter, and any required changes.

I know we committed to tight timelines, but it would be great if we can deliver. If we can work on the 3 bullets above by the 1<sup>st</sup> of November, we really will be in good shape to have all of our deliverables finalized (per our group) before the year-end holidays, and allow review by the larger group before we all meet in Ghana.

If anyone feels a telecon would be helpful at any point in the process (this entire group, or a subset), please let me know and we will work to arrange.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Bailey, Steven R.

**Sent:** Wednesday, September 30, 2015 4:48 PM

**To:** Holm Karin; Bachtiar, Novilia (novilia@biofarma.co.id); Bergman, Ulf (b)(6); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Darko, Mimi (b)(6); DeStefano, Frank (fxd1@cdc.gov); Duo, Dong (dongduo@cdr.gov.cn); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); Maure, Christine (maurec@who.int); Menezes, Reinaldo de (Rmenezes@bio.fiocruz.br); Nishioka, Sergio (b)(6); Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Seifert, Harry (Harry.A.Seifert@gsk.com); Sjolín\_Forsberg Gunilla; Tebaa, Amina (b)(6); Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov); Zuber, Patrick (zuberp@who.int)

**Cc:** Ashley Wivel (ashley.wivel@merck.com); Maroko, Robert; Bailey, Steven R.

**Subject:** Some Meeting Follow Up

All (Primarily TG 2 members and key stakeholders)

Please find attached some promised documents (sorry for the delay).

Attached are:

- 1) The Updated Business Plan for TG2. Please pay special attention to your assignments and due dates in the business plan. I will send reminders in about 2 weeks to try to keep us on track. Please feel free to offer updates or suggestions if I missed anything.
- 2) Attached is our preliminary RACI. Will require more work as we move forward, but a good start.
- 3) The latest draft of the Introduction that we discussed at the meeting. Ashley, Rob, Scott and others who offered to work on this (including myself), please compare against the business plan for what we agreed to as next steps. If anyone feels a small telecon to further discuss the intro is needed, do not hesitate to request, and I can arrange.

It was a pleasure seeing most of you in Collegeville, and for those who could not attend, look forward to seeing you in Ghana. I will trust everyone will move forward with our work as outlined in the business plan, and will check in in a few weeks. If any questions, please reach out.

Regards,



Steven

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Holm Karin [<mailto:holmkarin@cioms.ch>]

**Sent:** Thursday, September 24, 2015 11:03 AM

**To:** Abdoellah, Siti (alt) ([\(b\)\(6\)](#)); Arlett, Peter ([Peter.Arlett@ema.europa.eu](mailto:Peter.Arlett@ema.europa.eu)); Ayoub, Ayman; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Bailey, Steven R.; Benkirane, Raja ([\(b\)\(6\)](#)); Bergman, Ulf ([\(b\)\(6\)](#)); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)); Bonhoeffer, Jan (alt) ([j.bonhoeffer@brightoncollaboration.org](mailto:j.bonhoeffer@brightoncollaboration.org)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Ceuppens, Marc ([mceuppe1@its.jnj.com](mailto:mceuppe1@its.jnj.com)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mimi ([\(b\)\(6\)](#)); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ([alex.dodoo@umcafrica.org](mailto:alex.dodoo@umcafrica.org)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Gregory, William (NYC); Gunale, Bhagwat (alt) ([bhagwat.gunale@seruminstitute.com](mailto:bhagwat.gunale@seruminstitute.com)); HAMID, T. Bahdar Johan ([\(b\)\(6\)](#)); Heiles, Bernhard ([bernhard.heiles@merck.com](mailto:bernhard.heiles@merck.com)); Heininger, Ulrich ([ulrich.heininger@ukbb.ch](mailto:ulrich.heininger@ukbb.ch)); Holm Karin; Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Keller-Stanislawski ([Brigitte.Keller-Stanislawski@pei.de](mailto:Brigitte.Keller-Stanislawski@pei.de)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kulkarni, Prasad ([drpsk@seruminstitute.com](mailto:drpsk@seruminstitute.com)); Kurz, Xavier ([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Lindquist, Marie ([Marie.Lindquist@who-umc.org](mailto:Marie.Lindquist@who-umc.org)); Martin, David ([David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Mentzer, Dirk ([Dirk.Mentzer@pei.de](mailto:Dirk.Mentzer@pei.de)); Nishioka, Sergio ([\(b\)\(6\)](#)); Nohynek Anna ([Hanna.Nohynek@thl.fi](mailto:Hanna.Nohynek@thl.fi)); Oberle, Doris (alt2) ([Doris.Oberle@pei.de](mailto:Doris.Oberle@pei.de)); Patel, Mayur (alt) ([PatelMayur@MedImmune.com](mailto:PatelMayur@MedImmune.com)); Ramkishan, Ajmeer ([\(b\)\(6\)](#)); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Shimabukuro, Tom (alt) ([ayv6@cdc.gov9](mailto:ayv6@cdc.gov9)); Sjolín Forsberg Gunilla; Srivastava, Swati (alt) ([\(b\)\(6\)](#)); Tebaa, Amina ([\(b\)\(6\)](#)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Youssef, Mona ([\(b\)\(6\)](#)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Le\_Roux Susanne; Habersaat, Katrine (DCE-VPI); Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert

**Subject:** Philly meeting group photo

Dear All,

Sending you the group photo from the Philadelphia meeting, which I think reflects on our faces the positive feelings we had about what we achieved at this meeting.

I will also shortly be sending you information about how to access the SharePoint website in an easier manner to get the latest drafts and background documents (I have not yet posted all the updates but shall in coming few weeks).

You will also receive within the coming few weeks, the Philly meeting report so that everyone will feel up-to-date and ready to contribute to this next phase of further writing and editing. Even if you have had little time to involve yourself until now, the Editorial Team can really use your help, expertise, and support to produce a useful guide to Vaccine Safety for new and new-to-you (as we were calling them for short) vaccines.

Please be already planning on attending the next 8<sup>th</sup> meeting to be hosted in Accra, Ghana by the Ghana Food and Drugs Authority, in March or April 2016, as announced by Mimi Darko on the second day of our meeting. We will be sending out a doodle to help determine the best date.

Best regards,  
Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holm@cioms.ch](mailto:holm@cioms.ch)

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(b)(4)

(b)(4)



(b)(4)

(b)(4)

(b)(4)

**From:** Bailey, Steven R.  
**Sent:** Tue, 15 Dec 2015 16:19:40 +0000  
**To:** Wivel, Ashley E.;Corinne.Jouquelet-Royer@sanofipasteur.com;Destefano, Frank (CDC/OID/NCEZID);Winiecki, Scott (FDA/CBER);holmk@cioms.ch;novilia@biofarma.co.id (b)(6);Irina.Caplanusi@em a.europa.eu;mimidarko66@yahoo.co.uk;dongduo@cdr.gov.cn;maurec@who.int;Rmenezes@bio.fiocruz .br (b)(6);Paulo.santos@bio.fiocruz.br;Harry.A.Seifert@gsk.com;sjolin@orsbergg@cioms.ch;atebaa@yahoo.fr;Zuber, Patrick (CDC who.int)  
**Cc:** Maroko, Robert;dongduo@cdr-adr.org.cn;董铎;Bailey, Steven R.  
**Subject:** RE: Some Meeting Follow Up  
**Attachments:** CIOMS Manual on Vaccine Active Safety Surveillance All Comments Combined Chapt 1 update srb.docx  
**Importance:** High

All:

In follow up to the below, please find attached a version of our section with an update to Chapter 1. I have gone through the chapter, and made the suggested edits (and dealt with conflicting edits), as well as addressing all comments. The result is a "near final" draft that would be ready for review by the larger CIOMS group when we have all sections updated.

(b)(4)

If I can, I would suggest the other section authors do the same. Once we have collected all of the sections, we can put them into one document, and all the open questions for team discussion will be in one place. We can then either a) meet ahead of Ghana by telecon to resolve them or b) wait for discussion at Ghana.

My preference would be to try to schedule a telecon in February if the team agrees. That way we can have these items resolved ahead of the next meeting, and make that more productive.

Please let me know your preferences, and I will update our business plan appropriately.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Bailey, Steven R.

**Sent:** Tuesday, December 8, 2015 5:23 PM

**To:** 'Wivel, Ashley E.'; Corinne.Jouquelet-Royer@sanofipasteur.com; fxd1@cdc.gov;

Scott.Winiecki@fda.hhs.gov; holmk@cioms.ch; novilia@biofarma.co.id; (b)(6)

Irina.Caplanusi@ema.europa.eu; (b)(6); dongduo@cdr.gov.cn; maurec@who.int;

Rmenezes@bio.fiocruz.br; sergio.de.andrade.nishioka@gmail.com; Paulo.santos@bio.fiocruz.br;

Harry.A.Seifert@gsk.com; sjolinforsbergg@cioms.ch; (b)(6) zuberp@who.int

**Cc:** Maroko, Robert; dongduo@cdr-adr.org.cn; 董铎

**Subject:** RE: Some Meeting Follow Up

All (and esp. section owners):

I have combined all of the comments received to date into one document. (we have comments from Frank, Scott, Ashley, Steven, Mimi, Duo Dong, and Corinne). This combined document (it pulls together all the track changes and comments together in one place, which may make your updating of your chapters easier if you have done that already. And, if we all use this version, it may be a bit easier to put it all together when we are done. If everyone sticks to their chapters that they own, and address all the comments/changes, we can then merge the three documents together easily.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Wivel, Ashley E. [<mailto:ashley.wivel@merck.com>]

**Sent:** Sunday, November 29, 2015 11:28 PM

**To:** Bailey, Steven R.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);

[Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holmk@cioms.ch](mailto:holmk@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [ulfkabergman@hotmail.com](mailto:ulfkabergman@hotmail.com);

[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); [mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int);

[Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); [sergio.de.andrade.nishioka@gmail.com](mailto:sergio.de.andrade.nishioka@gmail.com); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br);

[Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforsbergg@cioms.ch](mailto:sjolinforsbergg@cioms.ch); [atebaa@yahoo.fr](mailto:atebaa@yahoo.fr); [zuberp@who.int](mailto:zuberp@who.int)

**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎

**Subject:** RE: Some Meeting Follow Up

Hi Steven

Thanks very much for the opportunity to review—I added few comments on the chapters for consideration by the chapter authors

Best regards,  
Ashley



---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]

**Sent:** Wednesday, November 18, 2015 9:26 AM

**To:** Wivel, Ashley E.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holmk@cioms.ch](mailto:holmk@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [ulfkabergman@hotmail.com](mailto:ulfkabergman@hotmail.com); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); [mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); [sergio.de.andrade.nishioka@gmail.com](mailto:sergio.de.andrade.nishioka@gmail.com); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforsbergg@cioms.ch](mailto:sjolinforsbergg@cioms.ch); [atebaa@yahoo.fr](mailto:atebaa@yahoo.fr); [zuberp@who.int](mailto:zuberp@who.int)

**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎

**Subject:** RE: Some Meeting Follow Up

Thanks Ashley. Actually this raises a good point: if anyone else is still planning on providing comments, could you let us all know when you plan on doing so. I think all the chapter owners would appreciate knowing when to expect the last comments, so they can efficiently update.

If anyone is still planning on sending comments on the completed section, please let us all know, and include when you will provide comments (and upon which version).

Many thanks,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Wivel, Ashley E. [<mailto:ashley.wivel@merck.com>]

**Sent:** Wednesday, November 18, 2015 9:21 AM

**To:** Bailey, Steven R.; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holmk@cioms.ch](mailto:holmk@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [ulfkabergman@hotmail.com](mailto:ulfkabergman@hotmail.com); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); [mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); [sergio.de.andrade.nishioka@gmail.com](mailto:sergio.de.andrade.nishioka@gmail.com); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolinforsbergg@cioms.ch](mailto:sjolinforsbergg@cioms.ch); [atebaa@yahoo.fr](mailto:atebaa@yahoo.fr); [zuberp@who.int](mailto:zuberp@who.int)

**Cc:** Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); 董铎

**Subject:** RE: Some Meeting Follow Up

Hi Steven

Thanks very much for keeping us on track and helping to coordinate the complex project. I plan to review the last version of the chapters (with comments from srb, skw, cjr) which was sent around recently and to add my comments by Monday 23 November at the latest(hopefully sooner!)

I will loop back with you and Rob separately to discuss the introduction

Best regards,

Ashley

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** Tuesday, November 17, 2015 5:43 PM  
**To:** [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [holm@cioms.ch](mailto:holm@cioms.ch); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); (b)(6); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); (b)(6); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [maurec@who.int](mailto:maurec@who.int); [Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br); (b)(6); [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [sjolin@forsbergg@cioms.ch](mailto:sjolin@forsbergg@cioms.ch); (b)(6); [zuberp@who.int](mailto:zuberp@who.int)  
**Cc:** Wivel, Ashley E.; Maroko, Robert; [dongduo@cdr-adr.org.cn](mailto:dongduo@cdr-adr.org.cn); Bailey, Steven R.; 董铎  
**Subject:** RE: Some Meeting Follow Up

All:

Just taking a status check to see where everything stands, and everyone's preferred next steps. I think we will need to adjust our business plan a bit (which is fine, we will still be ready for Ghana)

Here is current status of each item:

- 1) Thorough review of Latest Draft of All Chapters: Largely Complete: comments received from Corinne, Duo Dong, Steven, Frank, Scott, Mimi, and, perhaps someone I am missing.
- 2) Chapter 3, Table 3.3, Section 3.4: Novi has provided text to Irina. Awaiting further edits from Irina
- 3) Chapter 3, 3.5/3.6: Done. Scott provided to the entire group
- 4) Introduction: Intro/Algorithm/RACI: Complete and Circulated to Team. Comments Received
- 5) Introduction: Structured Approach: Ashley has completed a draft. Rob Maroko to review (and then I will review)
- 6) Ethical Section: Comments Received along with the comments (item 1 above).

Thanks to everyone who has provided authorship/comments to date. We are making good progress. If my summary above is up to date, the following are our next steps:

- 1) **Steven/Scott/Frank:** Update Chapters 1/2/3 with comments from others. I have not had time to complete this yet. **Frank** and **Scott:** what is the status for Chapter 2 and 3? We had originally said these would be complete by Nov 23<sup>rd</sup>. I will need at least until December 1<sup>st</sup>. Frank/Scott: is this workable for you? If not, simply propose a date and I will re-work our timelines appropriately (and Frank: see item 3 below)
- 2) **Irina:** Awaiting final text for section 3.4 and table 3.3. When do you think that will be ready? Once ready, we can circulate to the larger group.
- 3) **Frank:** once we have text from Irina (item 2), will you be able to incorporate this and the text from Scott for 3.6 into a final version of Chapter 3?
- 4) **Steven/Ashley/Rob:** **Rob:** when will you have reviewed the draft that Ashley provided? When complete, I will review and incorporate into a complete introduction. I will circulate to all at this point. I will aim for December 1<sup>st</sup> for this as well, or whatever date we land on for completion of all chapters.
- 5) **Someone (Volunteer Please):** The ethical section needs to be re-worked with all the comments received. While this currently sits in Chapter 3, but not sure it belongs there. It was not originally authored by Frank, and he has so much on his plate, that it would be helpful if



someone else would take on the rework of this section (and leading a discussion of where it best belongs).

Once I hear from everyone (and especially those **bolded** with todo items, including myself), I will re-work our business plan and dates for next steps. Ideally we will get everything roughly into the same timelines (Intro/Chapters 1-3/Additional Chapter 3 material/Ethical Section) probably by December 15<sup>th</sup> (earlier if everyone agrees, but hopefully before Christmas). If we can do this, then we will be able to relax over the holiday season, and we can circulate everything in the new year for one last look to our group and get this to everyone at least a month ahead of the meeting in Ghana.

Regards, and thanks,

Steven.

All:

We are just 1 week away from our first set of deadlines for TG2 (November 1<sup>st</sup> if a week from this Sunday), and I want to make sure we were moving along, and either encourage everyone to provide updates, or, if necessary, rework our deliverable date.

From our business plan, here is what is due by November 1<sup>st</sup>:

- Thorough review of Chapters 1, 2 and 3, with track changes/comments to Chapter owners **(ALL)**
- Chapter 3: Table 3.3, Section 3.4: Update/Write: **(Novi/Irina)**
- Chapter 3: Sections 3.5 and 3.6: Update/Write: **(Scott)**
- Introduction: Update/Write section 1 (intro), section 2 (algorithm), section 3 (RACI): **(Steven)**
- Introduction: Write Section 4 (structure approach to reviewing data) **(Ashley/Rob (draft 1))**
- Ethical Section (end of chapter 3 now): Carefull Review/update: **(ALL)**

Per previous e-mail, I have already completed bullet 4 and circulated. I am now providing my thorough review of the first 3 chapters, with special attention to the ethical section (see attached).

Hoping this encourages everyone to move forward with the above. However, I do understand how busy schedules are, so let's see how everyone does over the coming week, and we can consider moving our deadlines as needed. Also, based on where we are, I would like to set up a telecon of the group in mid November or so to go over any open items or issues.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)



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**From:** Bailey, Steven R.

**Sent:** Monday, October 12, 2015 12:58 PM

**To:** Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bergman, Ulf (b)(6); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi (b)(6); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Nishioka, Sergio (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sjolín\_Forsberg Gunilla; Tebaa, Amin (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert; 'dongduo@cdr-adr.org.cn'

**Subject:** RE: Some Meeting Follow Up

**Importance:** High

All:

Hope everyone is well. I wanted to make sure we were still keeping up the momentum for TG2. So I have gone ahead and completed one of my deliverables for the project. Please find attached a DRAFT of an update to the Introduction. It includes 3 of the 4 pieces: the opening, the RACI, and the Algorithm.

The last piece of the intro is the (b)(4)

(b)(4)

Ashley and Rob have agreed to take a stab at adding this piece (first draft), and my hope is that by providing this it will be helpful in moving this forward. Ashley/Rob: please reach out if needed as we move this forward.

Please keep in mind the remaining activities per our business plan:

For November 1<sup>st</sup>:

- All to review Chapters 1, 2, and 3 very carefully. Please send your comments to all, and the owner of each section will consolidate those comments and provide the next draft. Please note the revised drafts are due November 23<sup>rd</sup>, so it is very important that you provide your comments by NOVEMBER 1<sup>st</sup>, as discussed. [as a reminder, Chapter Owners are Chapter 1: Steven, Chapter 2: Scott, Chapter 3: Frank]
- Novi/Irina/Scott: Chapter 3 has some sections that still need to be completed, and you all kindly "volunteered" to work on these sections (Table 3.3/section 3.4 (Irina/Novi) and section 3.5/3.6 (Scott))
- All: Review the "ethical section" of chapter 3, with an eye towards how it fits with the rest of the chapter, and any required changes.

I know we are committed to tight timelines, but it would be great if we can deliver. If we can work on the 3 bullets above by the 1<sup>st</sup> of November, we really will be in good shape to have all of our deliverables finalized (per our group) before the year-end holidays, and allow review by the larger group before we all meet in Ghana.

If anyone feels a telecon would be helpful at any point in the process (this entire group, or a subset), please let me know and we will work to arrange.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Bailey, Steven R.

**Sent:** Wednesday, September 30, 2015 4:48 PM

**To:** Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bergman, Ulf (b)(6); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi ([mimidarko66@yahoo.co.uk](mailto:mimidarko66@yahoo.co.uk)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Nishioka, Sergio (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Sjolín, Forsberg Gunilla; Tebaa, Amina (b)(6); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert; Bailey, Steven R.

**Subject:** Some Meeting Follow Up

All (Primarily TG 2 members and key stakeholders)

Please find attached some promised documents (sorry for the delay).

Attached are:

- 1) The Updated Business Plan for TG2. Please pay special attention to your assignments and due dates in the business plan. I will send reminders in about 2 weeks to try to keep us on track. Please feel free to offer updates or suggestions if I missed anything.
- 2) Attached is our preliminary RACI. Will require more work as we move forward, but a good start.
- 3) The latest draft of the Introduction that we discussed at the meeting. Ashley, Rob, Scott and others who offered to work on this (including myself), please compare against the business plan for what we agreed to as next steps. If anyone feels a small telecon to further discuss the intro is needed, do not hesitate to request, and I can arrange.

It was a pleasure seeing most of you in Collegeville, and for those who could not attend, look forward to seeing you in Ghana. I will trust everyone will move forward with our work as outlined in the business plan, and will check in in a few weeks. If any questions, please reach out.

Regards,

Steven

Steven R. Bailey, MD MPH MBA



Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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**From:** Holm Karin [<mailto:holm@cioms.ch>]

**Sent:** Thursday, September 24, 2015 11:03 AM

**To:** Abdoellah, Siti (alt) (b)(6); Arlett, Peter ([Peter.Arlett@ema.europa.eu](mailto:Peter.Arlett@ema.europa.eu)); Ayoub, Ayman; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Bailey, Steven R.; Benkirane, Raja (b)(6); Bergman, Ulf (b)(6); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)); Bonhoeffer, Jan (alt) ([j.bonhoeffer@brightoncollaboration.org](mailto:j.bonhoeffer@brightoncollaboration.org)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Ceuppens, Marc ([mceuppe1@its.inj.com](mailto:mceuppe1@its.inj.com)); Chandler, Rebecca (alt) ([rebecca.chandler@who-umc.org](mailto:rebecca.chandler@who-umc.org)); Darko, Mimi (b)(6); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ([alex.dodoo@umcafrica.org](mailto:alex.dodoo@umcafrica.org)); Duo, Dong ([dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn)); Gregory, William (NYC); Gunale, Bhagwat (alt) ([bhagwat.gunale@seruminstitute.com](mailto:bhagwat.gunale@seruminstitute.com)); HAMID, T. Bahdar Johan (b)(6); Heiles, Bernhard <[bernhard.heiles@merck.com](mailto:bernhard.heiles@merck.com)>; Heininger, Ulrich ([ulrich.heininger@ukbb.ch](mailto:ulrich.heininger@ukbb.ch)); Holm Karin; Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Keller-Stanislawski ([Brigitte.Keller-Stanislawski@pei.de](mailto:Brigitte.Keller-Stanislawski@pei.de)); Kilpi, Terhi ([terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi)); Kulkarni, Prasad ([drpsk@seruminstitute.com](mailto:drpsk@seruminstitute.com)); Kurz, Xavier ([Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu)); Lindquist, Marie ([Marie.Lindquist@who-umc.org](mailto:Marie.Lindquist@who-umc.org)); Martin, David ([David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Menezes, Reinaldo de ([Rmenezes@bio.fiocruz.br](mailto:Rmenezes@bio.fiocruz.br)); Mentzer, Dirk ([Dirk.Mentzer@pei.de](mailto:Dirk.Mentzer@pei.de)); Nishioka, Sergio ([sergio.de.andrade.nishioka@gmail.com](mailto:sergio.de.andrade.nishioka@gmail.com)); Nohynek Anna ([Hanna.Nohynek@thl.fi](mailto:Hanna.Nohynek@thl.fi)); Oberle, Doris (alt2) ([Doris.Oberle@pei.de](mailto:Doris.Oberle@pei.de)); Patel, Mayur (alt) ([PatelMayur@MedImmune.com](mailto:PatelMayur@MedImmune.com)); Ramkishan, Ajmeer (b)(6); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Seifert, Harry ([Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com)); Shimabukuro, Tom (alt) ([ayv6@cdc.gov](mailto:ayv6@cdc.gov)); Sjolín, Forsberg Gunilla; Srivastava, Swati (alt) (b)(6); Tehaa, Amina ([atehbaa@yahoo.fr](mailto:atehbaa@yahoo.fr)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Youssef, Mona (b)(6); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Cc:** Le\_Roux Susanne; Habersaat, Katrine (DCE-VPI); Ashley Wivel ([ashley.wivel@merck.com](mailto:ashley.wivel@merck.com)); Maroko, Robert

**Subject:** Philly meeting group photo

Dear All,

Sending you the group photo from the Philadelphia meeting, which I think reflects on our faces the positive feelings we had about what we achieved at this meeting.

I will also shortly be sending you information about how to access the SharePoint website in an easier manner to get the latest drafts and background documents (I have not yet posted all the updates but shall in coming few weeks).

You will also receive within the coming few weeks, the Philly meeting report so that everyone will feel up-to-date and ready to contribute to this next phase of further writing and editing. Even if you have had little time to involve yourself until now, the Editorial Team can really use your help, expertise, and support to produce a useful guide to Vaccine Safety for new and new-to-you (as we were calling them for short) vaccines.

Please be already planning on attending the next 8<sup>th</sup> meeting to be hosted in Accra, Ghana by the Ghana Food and Drugs Authority, in March or April 2016, as announced by Mimi Darko on the second day of our meeting. We will be sending out a doodle to help determine the best date.

Best regards,  
Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holm@cioms.ch](mailto:holm@cioms.ch)

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**From:** Bailey, Steven R.  
**Sent:** Fri, 26 Dec 2014 20:12:46 +0000  
**To:** Holm Karin; Antonia Utami; Arlett, Peter; Ayoub, Ayman; Bachtiar, Novilia; Benkirane (b)(6); Blum, Michael (BlumM@MedImmune.com); Bonhoeffer, Jan (j.bonhoeffer@brightoncollaboration.org); Brigitte.Keller-Stanislawski@pei.de; Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu); Ceuppens, Marc (mceuppe1@its.jnj.com); Darko, Mimi (b)(6); Dawei, Liu (liudw929@126.com); Destefano, Frank (CDC/OID/NCEZID); Dodoo, Alex UMC; Duo, Dong (dongduo@cdr.gov.cn); Gunale, Bhagwat (alt) (bhagwat.gunale@seruminstitute.com); Hartigan-Go, Kenneth; Heininger (ulrich.heininger@ukbb.ch); Joan Benson (alt) (joan\_benson@merck.com); Jouquelet-Royer, Corinne; Kulkarni, Prasad (drpsk@seruminstitute.com); Lievano, Fabio (alt) (fabio\_lievano@merck.com); Lindquist, Marie; Martin, David (FDA/CBER); Maure, Christine (maurec@who.int); Mentzer, Dirk (Dirk.Mentzer@pei.de); 'Nishioka, Sergio'; Nohynek Anna (Hanna.Nohynek@thl.fi); Oberle, Doris (alt2); Owden Amanda; PatelMayur@MedImmune.com; Peter Glen Y. Chua (peterchuamd@gmail.com); Ramkishan, Ajmeer (b)(6); Rauscher, Martina (MRausche@its.jnj.com); Reinaldo Menezes (Rmenezes@bio.fiocruz.br); Santos (alt) (Paulo.santos@bio.fiocruz.br); Seifert, Harry (Harry.A.Seifert@gsk.com); Shimabukuro, Tom (CDC/OID/NCEZID); Sillan, Françoise (Francoise.Sillan@sanofipasteur.com); Siti Asfijah Abdoellah (alt); Sjolín\_Forsberg Gunilla; sten.olsson@who-umc.org; swati srivastava (alt) (b)(6); Tebaa, Amina; terhi.kilpi@thl.fi; Bergman Ulf; Gregory, William (NYC); Winiecki, Scott (FDA/CBER); Xavier.Kurz@ema.europa.eu; Youssef, Mona (b)(6); Zuber, Patrick (CDC who.int)  
**Cc:** Ingemar Persson (ingemarpersson@me.com)  
**Subject:** RE: CIOMS ActSS Chapters 1-3  
**Attachments:** Ch1-VM2-141222\_kh.docx

All:

First, best wishes to all for a very happy, and hopefully productive, new year in 2015.

Ahead of our telecon scheduled for January 8<sup>th</sup>, I have been reviewing the draft of Chapter 1 (included in the message from Karin, and included here for ease of review. We have made good progress on this chapter (as well as chapters 2 and 3). There are a few items of note (alluded to in the comments in this version), which will require discussion by the larger WG, and we look forward to these discussion on the 8<sup>th</sup>.

However, there is a larger issue with Chapter 1, and one which is critical to our work moving forward: the need for examples of the types of knowledge gaps and/or issues that would arise with vaccine introduction in LMICs that would warrant active surveillance. These example are really the key to the chapter, and set the stage for the rest of the manual. It is critical that we make sure we have good examples for this introductory chapter, and that we all agree (more or less) that we have a good list of the types of issues and gaps that are pertinent to the need for active safety surveillance in LMICs.

Therefore, it is critical that we begin to align around the examples (whether all are applicable, and whether any have not been identified). We will certainly be able to discuss this on the 8<sup>th</sup>, but to make this session as productive as possible (we have only an hour for Chapters 1 and 2), it would be very



helpful that everyone be prepared to discuss the issues of special importance to LMICs (the numbered sections beginning at the bottom of page 5). If possible to forward examples for each of the issues that have already been identified or offer new ones **AHEAD** of the meeting, copying the group, that would be esp. helpful, as we could begin to incorporate ahead of the meeting and use the limited time left for Ingemar (and it would allow input from those who are not attending). But at minimum we would really appreciate readiness for discussion of this section from all, and especially from our colleagues in the LMICs themselves to help ensure we have identified the key issues, which will set the stage for the manual to follow.

Thanks in advance for you inputs, and looking forward to talking with everyone in about 2 weeks.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmkarin@cioms.ch]  
**Sent:** Tuesday, December 23, 2014 10:45 AM  
**To:** Antonia Utami ; Arlett, Peter; Ayoub, Ayman; Bachtiar, Novilia; Bailey, Steven R.; Benkirane (b)(6); Blum, Michael (BlumM@MedImmune.com); Bonhoeffer, Jan (j.bonhoeffer@brightoncollaboration.org); Brigitte.Keller-Stanislawski@pei.de; Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu); Ceuppens, Marc (mceuppe1@its.jnj.com); Darko, Mimi (b)(6); Dawei, Liu (liudw929@126.com); DeStefano, Frank (fxd1@cdc.gov); Dadoo, Alex UMC; Duo, Dong (dongduo@cdr.gov.cn); Gunale, Bhagwat (alt) (bhagwat.gunale@seruminstitute.com); Hartigan-Go, Kenneth; Heininger (ulrich.heininger@ukbb.ch); Holm Karin; Joan Benson (alt) (joan\_benson@merck.com); Jouquelet-Royer, Corinne; Kulkarni, Prasad (drpsk@seruminstitute.com); Lievano, Fabio (alt) fabio\_lievano@merck.com; Lindquist, Marie; Martin (David.Martin@fda.hhs.gov); Maure, Christine (maurec@who.int); Mentzer, Dirk (Dirk.Mentzer@pei.de); 'Nishioka, Sergio'; Nohynek Anna (Hanna.Nohynek@thl.fi); Oberle, Doris (alt2); Owden Amanda; PatelMayur@MedImmune.com; Peter Glen Y. Chua (b)(6); Ramkishan, Ajmeer (b)(6); Rauscher, Martina (MRausche@its.jnj.com); Reinaldo Menezes (Rmenezes@bio.fiocruz.br); Santos (alt) (Paulo.santos@bio.fiocruz.br); Seifert, Harry (Harry.A.Seifert@gsk.com); Shimabukuro, Tom ; Sillan, Françoise (Francoise.Sillan@sanofipasteur.com); Siti Asfijah Abdoellah (alt); Sjolín\_Forsberg Gunilla; sten.olsson@who-umc.org; swati srivastava (alt) (b)(6); Tebaa, Amina; terhi.kilpi@thl.fi; Bergman Ulf; Gregory, William (NYC); Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov); Xavier.Kurz@ema.europa.eu; Youssef, Mona (b)(6); Zuber, Patrick (zuberp@who.int)  
**Cc:** Ingemar Persson (ingemarpersson@me.com)  
**Subject:** CIOMS ActSS Chapters 1-3

Dear CIOMS WG on Vaccine Safety  
(and especially those in TG2 who are working on the Manual for Active Safety Surveillance)

Ingemar has now prepared a new 'master version of the first three chapters, where he has:

- tried to include all comments received so far (please tell us if we missed something!)
- incorporated contributions, e.g. case study examples
- enumerated the various paragraphs and subsections
- looked in a first step at consistency

His idea is that all new suggestions from comments could be incorporated in these 'VM2' (VersionMaster2) documents. N.B. that there are a number of remaining requests in the texts, highlighted in yellow. I have not had time to work on Ch 4.

It may be useful to see these 'master versions' and make comment directly in these.

Note that he will have 2 more days at a maximum after the **TC January 8 (9am-12 U.S Eastern Time)**. So please everyone, do your homework and read these, provide comments, prepare questions to discuss during the TC. This is really an important meeting so I will be sending you and Invite and Instructions you must install ahead of time – if you don't already have the set up for WebEx MeetMe(a Cisco product widely-used).

Best regards,  
Karin

**Karin R. Holm**

Publications Consultant, WG IX Risk Minimisation  
Technical Coordinator, WG on Vaccine Safety  
Council for International Organizations of Medical Sciences (CIOMS)  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)  
*Associate partner of UNESCO*  
*In official relations with WHO*

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**From:** Bailey, Steven R.  
**Sent:** Tue, 7 Oct 2014 02:39:36 +0000  
**To:** Michael Blum (BlumM@medimmune.com); Martin, David (FDA/CBER); Harry.A.Seifert@gsk.com; Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Rantz, Reggie; Bailey, Steven R.  
**Subject:** Follow Up from the CIOMS Meeting

Dear Mike/David/Frank/Harry:

As you may have heard, we had a successful meeting in Rabat. After discussion, we did make some important progress.

I have been asked by Gunilla and Karin to provide you all with a "personal" update to give you some insight into where we landed, and some new chapters we will be working on. They thought it best that I update all the Americans who were unable to attend.

I would like to set up a ½ hour telecon to get everyone to go over the Rabat meeting in the coming weeks. Could you all please provide Reggie and I some potential times/days that would work for you, and hopefully we can find a time that will work for everyone.

Kind regards, and look forward to talking to you soon,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

**From:** Corinne.Jouquelet-Royer@sanofipasteur.com  
**Sent:** Mon, 23 Mar 2015 16:47:25 +0000  
**To:** holmk@cioms.ch; Steven.R.Bailey@pfizer.com; Winiecki, Scott (FDA/CBER); mimidarko66@yahoo.co.uk; Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: CIOMS Comments on Ch1-3, from TG2 meeting discussions Ingemar Persson  
**Attachments:** Business Plan 19 March 2015.pptx

Dear Karin

Here is the business plan of TG2. Would be good if you could compile the business plans of each TG together and also include the slide you developed with the skeleton of the book. And circulate to all TGs. Thank you  
Co

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**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** lundi 23 mars 2015 16:44  
**To:** Bailey (Steven.R.Bailey@pfizer.com); Jouquelet-Royer, Corinne (sanofi pasteur); Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov); Darko, Mimi (mimidarko66@yahoo.co.uk); DeStefano, Frank (fxd1@cdc.gov)  
**Subject:** CIOMS Comments on Ch1-3, from TG2 meeting discussions Ingemar Persson

Dear Steven, Corinne, Mimi, Scott, and Frank,  
Attached please find comments for chapters 1-3 from Ingemar Persson based on the Lyon meeting.  
Karin

**Karin R. Holm**  
Publications Consultant, WG IX Risk Minimisation  
Technical Coordinator, WG on Vaccine Safety  
Council for International Organizations of Medical Sciences (CIOMS)  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)  
*Associate partner of UNESCO*  
*In official relations with WHO*

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**From:** Ingemar Persson [mailto:ingemarpersson@me.com]  
**Sent:** 23 March 2015 14:38  
**To:** Holm Karin  
**Cc:** Sjolín\_Forsberg Gunilla  
**Subject:** Comments on Ch1-3, from TG2 meeting discussions

Dear Karin,

Thanks for a good and fruitful meeting in Lyon last week. This my first time experience of a TG meeting was indeed positive. I think good progress was made and that important steps forward were taken. Also thanks to CIOMS for the nice dinner and pleasant social environment.



Corinne and Gunilla asked me to feed back to the group some comments from the discussion in the TG2. Please find attached my comments to the chapters based on what I captured from the discussions. Surely, I may have missed or misunderstood things, however my comments are given for further considerations by the TG2 group.

I trust that the chapter manuscripts will move forward with the defined work pieces and under the topic leads, based on the strategic decisions made at the meeting. I believe that the editorial board will have an important role eventually. I found the decided business plans very useful.

So, my best wishes for good progress in the TGs. Please do not hesitate to return to me should there be a need for further clarification.

The attached draft manuscript versions build on VM6 master documents previously sent out and tabled at the meeting, now revised and provided with my comments. The new names are: **Ch1-VM7-150319, Ch2-VM7-150319, Ch3-VM7-150319.**

Karin, please circulate the documents to the TG2 as you see needed. Maybe, Corinne, Steven, Mimi, Scott and Frank should take a first look before sending the drafts on.

My very best regards, thanks

Ingemar.

\*\*\*\*\*  
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\*\*\*\*\*

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**From:** Bailey, Steven R.  
**Sent:** Mon, 12 Jan 2015 10:07:26 +0000  
**To:** Holm Karin; Winiecki, Scott (FDA/CBER); Destefano, Frank (CDC/OID/NCEZID); Ingemar Persson (ingemarpersson@me.com); Bramley (david@bramley.ch); gunilla.sjolin-forsberg@mpa.se; Sjolin\_Forsberg Gunilla  
**Subject:** RE: Notes from TC and updated documents.

Karin:

Some suggested changes in the notes in red below.

Thanks for your excellent notes.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** Saturday, January 10, 2015 7:52 AM  
**To:** Bailey, Steven R.; Winiecki, Scott; 'Destefano, Frank (CDC/OID/NCEZID)'; Ingemar Persson (ingemarpersson@me.com); Bramley (david@bramley.ch); gunilla.sjolin-forsberg@mpa.se; Sjolin\_Forsberg Gunilla  
**Subject:** Notes from TC and updated documents.

Steven, Scott, Frank, Ingemar, David, Gunilla, -- for your review & edits. Would like to send out Monday or Tues if possible.

Dear CIOMS WG on Vaccine Safety,

We had a very productive TC on 8 January with 23 participants (connecting at various times during the three hours scheduled) including: Ayman, Christine, David Bramley, Fabio, Frank, Gunilla, Harry, Ingemar, Irina, Martina, Mayur, Michael, Novilia, Patrick, Paulo, Reinaldo, Scott, Sergio, Siti (she could listen but couldn't get her speaker to work on the call), Steven, Terhi, Xavier.

A big thank you to Steven for arranging through Pfizer's btconferencing. At least 90% also had access to the WebEx document-sharing which was quite helpful.

We covered some important issues and answered some but not yet all of Ingemar's questions as he highlighted in the latest versions of Ch. 1,2,3 of TG2's manual. We made progress on the

TG1 dossier/template but perhaps not enough to allow David Bramley, the Technical Editor, to fulfill his mission by 15 January.

Here are my notes and the attached documents. Please let me know if there are any omissions, errors, additions.

CIOMS WG on Vaccine Safety – Major Issues Discussed on TC 8 Jan 2015  
Notes by Karin Holm

(b)(4)

(b)(5)



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(b)(5)

(b)(5)

**From:** Corinne.Jouquelet-Royer@sanofipasteur.com  
**Sent:** Fri, 5 Sep 2014 15:23:33 +0000  
**To:** Francoise.Sillan@sanofipasteur.com;maurec@who.int;holmk@cioms.ch;mimidarko66@yahoo.co.uk;Harry.A.Seifert@gsk.com;bergmanu@cioms.ch;Steven.R.Bailey@pfizer.com;BlumM@MedImmune.com;atebaa@yahoo.fr;novilia@biofarma.co.id;terhi.kilpi@thl.fi;Winiecki, Scott (FDA/CBER);sten.olsson@who-umc.org;dongduo@cdr.gov.cn;Destefano, Frank (CDC/OID/NCEZID);Irina.Caplanusi@ema.europa.eu;Xavier.Kurz@ema.europa.eu;liudw929@126.com;david.martin@ema.europa.eu  
**Cc:** sjolinforsbergg@cioms.ch;Zuber, Patrick (CDC who.int);sergio.nishioka@saude.gov.br  
**Subject:** Draft TOC of 5.4 for comment - Deadline Monday 8 Sept EOB  
**Attachments:** 5.4 draft.docx  
**Importance:** High

Dear all

You will find attached the draft TOC for section 5.4. Your comments are welcome.

I'm also expecting additional volunteers!!!

Deadline **Monday 8 Sept EOB**

Thank you. Have a nice weekend

Co

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**From:** Sillan, Francoise (sanofi pasteur)  
**Sent:** vendredi 5 septembre 2014 16:15  
**To:** 'MAURE, Christine'; Holm Karin; Jouquelet-Royer, Corinne (sanofi pasteur); Darko, Mimi (mimidarko66@yahoo.co.uk); Seifert, Harry; Bergman Ulf; Bailey (Steven.R.Bailey@pfizer.com); Blum, Michael (BlumM@MedImmune.com); Tebaa, Amina; Bachtiar, Novilia; terhi.kilpi@thl.fi; Winiecki, Scott; sten.olsson@who-umc.org; Duo, Dong; DeStefano, Frank; Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu); Xavier.Kurz@ema.europa.eu; Dawei, Liu (liudw929@126.com); david.martin@ema.europa.eu  
**Cc:** Sjolín\_Forsberg Gunilla; ZUBER, Patrick Louis F.; Nishioka, Sergio  
**Subject:** Update TG2: Overall Fri, 3pm

Dear all

As discussed today I send you updated version of the power point presentation of the business plan and a word document on the TOC for the manual including some instructions for the sections as decided during our previous meeting in UPSSALA.

Do not hesitate if you have any comment on the content of the document.

Thank you again for your contribution.

*Best regards << File: TG2 business plan Sept 5.pptx >> << File: CIOMS Manual active safety surveillance.docx >>*

*Françoise*

---

**De :** Sillan, Françoise (sanofi pasteur)

**Envoyé :** vendredi 5 septembre 2014 12:04

**À :** 'MAURE, Christine'; Holm Karin; Jouquelet-Royer, Corinne (sanofi pasteur); Darko, Mimi (mimidarko66@yahoo.co.uk); Seifert, Harry; Bergman Ulf; Bailey (Steven.R.Bailey@pfizer.com); Blum, Michael (BlumM@MedImmune.com); Tebaa, Amina; Bachtiar, Novilia; terhi.kilpi@thl.fi; Winiecki, Scott; sten.olsson@who-umc.org; Duo, Dong; DeStefano, Frank; Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu); Xavier.Kurz@ema.europa.eu; Dawei, Liu (liudw929@126.com); david.martin@ema.europa.eu

**Cc :** Sjolín\_Forsberg Gunilla; ZUBER, Patrick Louis F.; Nishioka, Sergio

**Objet :** TG2: Overall Fri, 3pm

<< Fichier: TG2 business plan Sept 5.pptx >>

Dear all

Please find enclosed some slides to prepare the TC today.

**Françoise SILLAN**

QPPV

Global Pharmacovigilance

TÉL. : +33 (0)4.37.37.78. 64 - MOB. : +33 (0)6.30.48.91.32

SIÈGE MONDIAL - 2, AVENUE PONT PASTEUR - 69367 LYON cedex 07 - France



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\*\*\*\*\*

<b>1. Ethical conduct , patient and data protection</b>	<b>Karin</b>
<b>2. Conduct and oversight of the study</b>	<b>Corinne</b>
Protocol and design	<b>Corinne</b>
Review of the protocol	<b>Corinne</b>
Approval of the study	<b>Corinne</b>
Monitoring	<b>Corinne</b>
<b>3. Role of the stakeholders</b>	
Sponsor	<b>Corinne</b>
Safety Expert Group	<b>Patrick</b>
National authorities : (1) Regulators; (2) Public Health Agency/ Immunization Programm	<b>Mimi</b>
GACVS	<b>WHO (?)</b>
<b>4. Communication</b>	<b>To be discussed at the workshop in Rabat</b>

### **Ethical conduct , patient and data protection**

According human research, irrespective of the design should be carried out according to high ethical, medical and scientific standards.

### **Oversight of the study**

Protocol and design

Review of the protocol

Approval of the study

Monitoring

### **Role of the stakeholders**

Sponsor

Expert Group

National authorities

GACVS

## **Resources**

[Link to templates and existing guidances](#)

In order to define in which circumstances active safety surveillance would be necessary all stakeholders should:

Have a shared understanding of the existing safety data at the time of market introduction

Understand the existing identified risks and the proposed minimization measures

Possible gaps related to special populations



**From:** Francoise.Sillan@sanofipasteur.com  
**Sent:** Fri, 5 Sep 2014 10:03:41 +0000  
**To:** maurec@who.int; holmk@cioms.ch; Corinne.Jouquelet-Royer@sanofipasteur.com; mimidarko66@yahoo.co.uk; Harry.A.Seifert@gsk.com; bergmanu@cioms.ch; Steven.R.Bailey@pfizer.com; BlumM@MedImmune.com; atebaa@yahoo.fr; novilia@biofarma.co.id; terhi.kilpi@thl.fi; Winiecki, Scott (FDA/CBER); sten.olsson@who-umc.org; dongduo@cdr.gov.cn; Destefano, Frank (CDC/OID/NCEZID); Irina.Caplanusi@ema.europa.eu; Xavier.Kurz@ema.europa.eu; liudw929@126.com; avid.martin@ema.europa.eu  
**Cc:** sjolinforbergg@cioms.ch; Zuber, Patrick (CDC who.int); sergio.nishioka@saude.gov.br  
**Subject:** TG2: Overall Fri, 3pm  
**Attachments:** TG2 business plan Sept 5.pptx

Dear all  
Please find enclosed some slides to prepare the TC today.

**Françoise SILLAN**

QPPV  
Global Pharmacovigilance  
TÉL. : +33 (0)4.37.37.78. 64 - MOB. : +33 (0)6.30.48.91.32  
SIÈGE MONDIAL - 2, AVENUE PONT PASTEUR - 69367 LYON cedex 07 - France



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\*\*\*\*\*



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**From:** Bailey, Steven R.  
**Sent:** Wed, 3 Jun 2015 19:05:54 +0000  
**To:** Winiecki, Scott (FDA/CBER);Corinne.Jouquelet-Royer@sanofipasteur.com;Caplanusi, Irina;Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: CIOMS active surveillance manual, Chapter 2

Scott:

I have reviewed again, and have nothing more at this point. You addressed my previous comments.

I would say it is good to go to next step of review as soon as you have comments back from the others on this e-mail.

Once question for this group: Rather than forward to Karin for distribution (to the entire CIOMS group), wouldn't it be better to include just our Topic Group for the time being? This is what I did with Chapter 1. I thought we would share with TG2 only, get their feedback then send to everyone in August ahead of our next F:F meeting. (by which time we might have drafts of all 3 chapters and could send them as a group).

(alternatively, if you go with the wider distribution, should probably do the same with Chapter 1. In that case, we could send them together).

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Winiecki, Scott [mailto:Scott.Winiecki@fda.hhs.gov]  
**Sent:** Friday, May 29, 2015 10:36 AM  
**To:** Bailey, Steven R.; Corinne.Jouquelet-Royer@sanofipasteur.com; Caplanusi, Irina; Destefano, Frank (CDC)  
**Subject:** CIOMS active surveillance manual, Chapter 2

Steven, Corinne, Irina, and Frank,  
I am attaching the most recent draft of Chapter 2. Steven did a quick read a couple of weeks ago and I made some changes based on his suggestions.

I would appreciate any comments/feedback you might have before I send this to Karin for wider distribution. It is only 7 pages, so it should not take too long.

Please respond by next Friday (5 June)if you have any suggestions.  
Thanks,

Scott

**From:** Francoise.Sillan@sanofipasteur.com  
**Sent:** Mon, 8 Sep 2014 16:43:36 +0000  
**To:** maurec@who.int; holmk@cioms.ch; Corinne.Jouquelet-Royer@sanofipasteur.com; (b)(6); Harry.A.Seifert@gsk.com; bergmanu@cioms.ch; Steven.R.Bailey@pfizer.com; BlumM@MedImmune.com; atebaa@yahoo.fr; novilia@biofarma.co.id; terhi.kilpi@thl.fi; Winiecki, Scott (FDA/CBER); sten.olsson@who-umc.org; dongduo@cdr.gov.cn; Destefano, Frank (CDC/OID/NCEZID); Irina.Caplanusi@ema.europa.eu; Xavier.Kurz@ema.europa.eu; liudw929@126.com; david.martin@ema.europa.eu  
**Cc:** sjolinforsbergg@cioms.ch; Zuber, Patrick (CDC who.int); sergio.nishioka@saude.gov.br  
**Subject:** RE: Update TG2: Overall Fri, 3pm  
**Attachments:** PMS\_AEFI Nov 1998.pdf, literature search\_active Safety surveillance.docx, active SS\_Singapore.pdf

Dear all

Last follow up of our TC, please find enclosed the literature search done at Sanofi Pasteur and some publications retrieved by Amina and by Chjristine.  
Please provide any additional publication which could be used to illustrate the section of this manual.

*Best regards  
Françoise*

---

**De :** Sillan, Francoise (sanofi pasteur)  
**Envoyé :** vendredi 5 septembre 2014 16:15  
**À :** 'MAURE, Christine'; 'Holm Karin'; Jouquelet-Royer, Corinne (sanofi pasteur); 'Darko, Mimi (b)(6)'; 'Seifert, Harry'; 'Bergman Ulf'; 'Bailey (Steven.R.Bailey@pfizer.com)'; 'Blum, Michael (BlumM@MedImmune.com)'; 'Tebaa, Amina'; 'Bachtiar, Novilia'; 'terhi.kilpi@thl.fi'; 'Winiecki, Scott'; 'sten.olsson@who-umc.org'; 'Duo, Dong'; 'DeStefano, Frank'; 'Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu)'; 'Xavier.Kurz@ema.europa.eu'; 'Dawei, Liu (liudw929@126.com)'; 'david.martin@ema.europa.eu'  
**Cc :** 'Sjolin\_Forsberg Gunilla'; 'ZUBER, Patrick Louis F.'; 'Nishioka, Sergio'  
**Objet :** Update TG2: Overall Fri, 3pm

Dear all

As discussed today I send you updated version of the power point presentation of the business plan and a word document on the TOC for the manual including some instructions for the sections as decided during our previous meeting in UPSSALA.

Do not hesitate if you have any comment on the content of the document.

Thank you again for your contribution.

*Best regards << Fichier: TG2 business plan Sept 5.pptx >> << Fichier: CIOMS Manual active safety surveillance.docx >>  
Françoise*

---

**De :** Sillan, Francoise (sanofi pasteur)

**Envoyé :** vendredi 5 septembre 2014 12:04

**À :** 'MAURE, Christine'; Holm Karin; Jouquelet-Royer, Corinne (sanofi pasteur); Darko, Mimi (mimidarko66@yahoo.co.uk); Seifert, Harry; Bergman Ulf; Bailey (Steven.R.Bailey@pfizer.com); Blum, Michael (BlumM@MedImmune.com); Tebaa, Amina; Bachtiar, Novilia; terhi.kilpi@thl.fi; Winiecki, Scott; sten.olsson@who-umc.org; Duo, Dong; DeStefano, Frank; Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu); Xavier.Kurz@ema.europa.eu; Dawei, Liu (liudw929@126.com); david.martin@ema.europa.eu

**Cc :** Sjolín\_Forsberg Gunilla; ZUBER, Patrick Louis F.; Nishioka, Sergio

**Objet :** TG2: Overall Fri, 3pm

<< Fichier: TG2 business plan Sept 5.pptx >>

Dear all

Please find enclosed some slides to prepare the TC today.

**Françoise SILLAN**

QPPV

Global Pharmacovigilance

TÉL. : +33 (0)4.37.37.78. 64 - MOB. : +33 (0)6.30.48.91.32

SIÈGE MONDIAL - 2, AVENUE PONT PASTEUR - 69367 LYON cedex 07 - France



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## Post-marketing surveillance for adverse events after vaccination: the national Vaccine Adverse Event Reporting System (VAERS)

### Learning Objectives:

Upon completion of this program, health professionals should be able to:

- Identify the principles of post-marketing surveillance
- Understand the objectives of VAERS
- Understand how VAERS operates
- Discuss basic limitations and strengths of data derived from VAERS
- List examples of FDA regulatory actions that have been based on post-marketing passive surveillance
- Describe how FDA disseminates information regarding vaccine safety to the public
- Understand how clinical practice impacts a national post-marketing surveillance system

### Faculty:

#### Manette T. Niu, MD

Medical Officer  
Epidemiology Branch  
Division of Biostatistics and  
Epidemiology (DBE)  
Center for Biologics Evaluation and  
Research (CBER), FDA

#### Marcel E. Salive, MD, MPH

Chief  
Epidemiology Branch  
Division of Biostatistics and  
Epidemiology (DBE)  
Center for Biologics Evaluation and  
Research (CBER), FDA

#### Susan S. Ellenberg, PhD

Director  
Division of Biostatistics and  
Epidemiology (DBE)  
Center for Biologics Evaluation and  
Research (CBER), FDA

### BENEFITS AND RISKS OF IMMUNIZATION

Over ten million childhood vaccinations are given to children (birth through 5 years) annually, and many million of doses are given to adults. All medicinal products, including vaccines, have risks and benefits. Vaccines protect many people from dangerous illnesses, but, like drugs, can cause side effects, a small percentage of which may be serious. The benefit of vaccines is measured as prevented disease, and the risk of vaccination is measured as potential side effects; both are monitored as part of the US public health system.

### PRE-LICENSURE EVALUATION OF VACCINES

Licensure requires extensive clinical evaluation of the vaccines' safety and effectiveness which is completed in stages over several years. First, laboratory and animal studies are performed. Then candidate vaccines are tested in small groups of adult volunteers to establish first the safety, and then, the efficacy of the vaccine. Finally larger-scale clinical trials, usually randomized and placebo-controlled, measure the rates of the more common adverse events and the protective efficacy of the vaccine. The control groups in these clinical trials who do not receive vaccine are critical to distinguishing between vaccine-related events and an event unrelated to vaccine but occurring spontaneously in the study population. Rates of the most common vaccine reactions, such as injection site reactions and fever, can be estimated before licensure, but the comparatively small number of patients enrolled in these trials generally limits detection of rare events or events that occur after long-term exposure. Even the largest pre-licensure trials (>10,000 persons) are inadequate to assess the vaccine's potential to induce rare but serious side effects. Consequently, it is essential

to continue to collect information on vaccine-associated adverse events after licensure which may only occur after wide-scale use of the vaccine in the general population.

### POST-MARKETING SURVEILLANCE

Post-marketing surveillance is a necessary component of vaccine safety monitoring. The manufacturers' label/product information approved at licensure has the potential to be continuously updated as significant adverse event information which differs from what was originally known at the time of approval is compiled. Due to the relatively small number of patients studied in pre-licensure studies, rarer side effects or events that may only occur in a sub-group of the population not significantly represented in pre-marketing studies (e.g., neonates and infants who receive hepatitis B vaccine, pregnant women, immunosuppressed patients), or side effects that occur only with chronic or repeated exposure to a vaccine-induced antigen may not be revealed until the vaccine is licensed to the general public.

Pre-licensing clinical trials are conducted in a controlled environment, much different from data obtained from passive or active post-marketing surveillance systems. After licensure, vaccinated persons have diverse demographic characteristics (e.g., age, race, socioeconomic background), medical history (immunocompromised host), and/or multiple medical problems necessitating medication (potential drug interactions). These previously unstudied components of a patient's social or medical history may be risk factors which could impact the outcome of vaccination and contribute to the development of adverse events. Thus, when the product leaves the controlled study environment of



clinical trials and is put into general clinical use by practitioners, the ability to determine the actual incidence of adverse events is questionable.

The objectives of post-marketing surveillance are to identify rare adverse reactions not detected during pre-licensure studies, monitor increases in known reactions, identify risk factors or pre-existing conditions that may promote reactions, and identify particular vaccine lots with unusually high rates or types of events.

There are two types of post-marketing surveillance systems typically in use: active and passive surveillance. Active surveillance links the vaccination status of all persons in a defined population to their clinical outcomes, thus, minimizing under-reporting. Such a system may provide comprehensive data, but may be very expensive and due to the comparatively small number of participants, may lack ability to detect very rare events or deaths. Passive surveillance systems rely on health professionals or vaccinees to voluntarily submit reports of illness following vaccination. There is no solicitation of these reports; this system is simpler, less expensive, does not limit the population from which reports are accepted, and because of the broad pool of reporters, offers the potential for detecting rare events. However, limitations of passive surveillance systems include variability in reporting standards, reporter bias and significant under-reporting of events. Both active and passive surveillance systems lack specificity, that is, reported post-vaccination events may be coincidental and not caused by the vaccine.

Associating causality of reported post-vaccination events with a specific vaccine is challenging and requires careful weighing of all the scientific evidence, evaluation of the quality and consistency of the data, and consideration of biologic plausibility of the association between vaccination and event (Table 1)(1,2,17). The stronger the vaccine-event relationship in each case, and rarer the spontaneous incidence of the event (i.e., background rate in an unvaccinated population), the fewer cases are needed to establish a causal association (1,2,17). Biologic plausibility

and strength of association aid in evaluating if an association is causal, as does a vaccination re-challenge ("positive rechallenge") which elicits an identical vaccine reaction (1,2).

When faced with a suspicious event, it is important to try to determine the background incidence rate of the event before making a judgement as to causality (1,2). Defining the relationship between vaccine exposure and the occurrence of an event is not easy, and it is often impossible with the available data to reach a conclusion. Since events may act through the same physiological and pathological pathways as normal disease, they are difficult to distinguish. The causal association between vaccination and event may be suggested by various criteria (Table 1)(1,2,17).

### VACCINE SAFETY SURVEILLANCE: VAERS

The National Childhood Vaccine Injury Act (NCVIA) of 1989 requires health professionals and vaccine manufacturers to report to the Department of Health and Human Services (DHHS) specific adverse events following the administration of vaccines specified in the Act. The Reportable Events Table, part of the Act, lists reportable post-vaccination events and the time frames in which they must occur in order to qualify as being reportable (Table 2)(17). In 1990, DHHS established the Vaccine Adverse Event Reporting System (VAERS), co-adminis-

tered by the Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC) to accept all reports of suspected adverse events after administration of any U.S. licensed vaccine.

VAERS, the national passive surveillance system monitoring vaccine safety, is a system to which clinical events after vaccination are voluntarily reported from health professionals, vaccine manufacturers, and the public (2,3). The reports are submitted to state or local public health authorities, vaccine manufacturers, or directly to VAERS, and all ultimately end up in the VAERS database. Food and Drug Regulations (21 CFR section 600.80) currently require that the following adverse events be reported to VAERS by each manufacturer having a product license from FDA: all spontaneous reports of adverse experiences occurring within the U.S., whether serious, non-serious, expected or unexpected; and all serious and unexpected adverse experiences occurring outside of the U.S. or reported in scientific/medical journals as case reports or as the result of formal clinical trials (Table 2)(17).

In order to encourage reporting of adverse events, FDA regulations offer substantial protection against disclosure of the identities of both reports and patients. Since July 3, 1995, a regulation preempted state discovery laws regarding voluntary

TABLE 1

#### EVALUATING SIDE EFFECTS AFTER VACCINATION: TEMPORAL VERSUS CAUSAL ASSOCIATIONS (17)

*An adverse event can be causally attributed to vaccine more readily if:*

1. Chronology of administration of agent, including beginning and ending of treatment and adverse event onset is known
2. Previously known toxicity of agent
3. Event conforms to a specific clinical syndrome whose association with vaccination has strong biologic plausibility (e.g., anaphylaxis)
4. Laboratory result confirms association (e.g., isolation of vaccine strain varicella vaccine from skin lesions of a patient with rash)
5. Event recurs on re-administration of vaccine ("positive rechallenge.")
6. Controlled clinical trial or epidemiologic study shows greater risk of adverse events among vaccinated vs unvaccinated (control) groups



reports held by pharmaceutical manufacturers.

## LIMITATIONS AND STRENGTHS OF VAERS

VAERS is subject to limitations inherent to passive surveillance systems (2,3). Nevertheless, the national VAERS has been successful in identifying vaccine-associated events that serve as hypotheses to be tested or further investigated in more rigorously controlled studies, such as the CDC's Vaccine Safety Datalink (VSD) (a computerized medical record linkage system of patients enrolled in 4 health maintenance organizations [HMOs]), where causality may be better determined (2-11).

### Limitations of VAERS

#### *Under-reporting*

VAERS receives only a portion of the total number of events ("numerator") which occur after vaccination (2,3,7,9,13). Computing reporting rates from VAERS may be misleading, since the extent of under-reporting is unknown. Compounding the problem of under-reporting is the lack of precise data as to the number of vaccine doses administered in the population ("denominator") or the number of persons at risk for the adverse event of interest. These limitations make incidence rates computed from spontaneously reported data problematic (2,3,7,9). In addition, VAERS does not receive reports for background events in unvaccinated persons--there is no control

group with whom to compare event rates in the vaccinated vs. unvaccinated population (2,3,9).

Given the limitations of VAERS (e.g., lack of accurate information as to the number of vaccine doses administered in the population, lack of control group, reporting bias, incomplete data, lack of consistent diagnostic criteria for disease, and indirect influences accorded sale of vaccine to government contracts in public sector and the manufacturers market share of vaccine), VAERS is a crude tool which may at best estimate reporting rates of events based on manufacturer distribution date (proprietary information available only to FDA and vaccine manufacturer), that serves as a signal suggesting hypotheses to test in methodologically more rigorous databases (2-11).

#### *Deficient data quality*

The ability to assess, analyze and act on safety issues based on spontaneous reporting is dependent on the quality of information submitted by reporters. Clinical details and diagnosis of a given report may be inaccurate, non-specific or missing. The quality of the data depends upon the reporter, who may lack clinical training, or who may not have access to complete clinical information. Since VAERS receives an estimated 12,000 reports annually, it is difficult to ensure the accuracy and completeness of the database with available resources, although checks are performed for a few key data items (e.g., type of vaccine, event severity).

### *Simultaneous administration of multiple vaccine antigens*

Following the current recommendations for childhood vaccines, reports often involve administration of multiple vaccine antigens, making identification of the role of a specific vaccine in an adverse event difficult (2,3,7,9).

#### *Reporting bias*

Spontaneously reported information is uncontrolled and subject to the possible influence of a number of biases that can affect reporting. Biases include length of time a product has been on the market (e.g., increased reporting rates the first 2 years a new vaccine is licensed), temporal reporting biases (e.g., events that occur within 4 weeks of vaccination are more likely to be reported) and reporting environment (e.g., increased reporting with news coverage and from the public vs private sector), individual biases (e.g., vaccinee convinced vaccine responsible for adverse event--initiating VAERS report or lawsuit)(2).

### *Inclusion of events not causally related to vaccination*

All reports are entered into the VAERS database regardless of confirmed or possible alternative explanations as to the cause of illness. Temporal association by itself does not mean that the vaccine caused a symptom or event as the event may be purely coincidental (1-3). Because of the large number of vaccine exposures, events temporally associated with vaccine will occur. With multiple childhood vaccines (diphtheria-tetanus-acellular pertussis [DTaP], oral polio virus [OPV]/inactivated polio virus [IPV], hemophilus influenzae type B virus [HIB]), administered to nearly all infants starting at two months of age, most health problems in infancy, whatever their cause, will occur in vaccinated children, some of which will by chance occur in recently vaccinated children (2).

An adverse event may be causally attributed to vaccination more readily if certain conditions are met (Table 1). Because few adverse events reported to VAERS meet these criteria, epidemiologic evidence is the basis for assessing causality for the most serious adverse events investigated. Determination if the vaccine caused the

TABLE 2

### ADVERSE EVENT (AE) REPORTING REQUIREMENTS FOR VACCINE MANUFACTURERS (17)

1. 15-day Alert reports: serious and unexpected (i.e., not in the product's current labeling) must be reported to FDA within 15 working days.
2. Periodic AE reports: all non-15 day AE reports must be reported periodically (quarterly for the first three years after approval, then annually).
3. Scientific literature: a 15-day report based on scientific literature (case report; results from a formal clinical trial; epidemiology-based studies or "analyses of experience in a monitored series of patients").
4. Post-marketing studies: pharmaceutical causation for AE "reasonable possibility."



post-vaccination event usually cannot be made on the basis of information acquired from individual VAERS reports, and needs confirmation in other methodologically more rigorous databases (e.g., VSD), or clinical trials (2,3,11).

### Strengths of VAERS

Although VAERS has methodologic limitations inherent in passive surveillance systems such as under-, biased-, and incomplete reporting, lack of consistent diagnostic criteria, lack of a comparison (control) group, and lack of data as to the precise number of doses of vaccine administered to the population, VAERS has strengths essential to the U.S. vaccine safety monitoring system (2,3). It is the only surveillance system which covers the entire U.S. population, includes the largest number of case reports of events temporally associated with vaccination in the U.S., and can assess the safety of specific vaccine lots. Other strengths include the timely availability of data from a geographically diverse population, the ability to detect possible new, unusual or rare adverse events and to generate hypotheses that may be tested in other databases (2,3). Spontaneous report-based surveillance programs perform an important function by generating signals of potential problems that may warrant further investigation.

VAERS is the “front line” of national vaccine safety surveillance and is especially valuable in assessing the safety of newly marketed vaccines and rare events (2,3). Careful review of reports during the initial months of licensed use can provide additional assurance about the safety of a new vaccine, uncover previously unexpected events which occur when a vaccine is used in a new sub-group, or rapidly identify problems not observed during pre-licensure. Recent reviews re-affirm the safety of hepatitis B vaccines in neonates and infants (7), and hepatitis A vaccine in the general population (8).

### OVERVIEW OF VAERS

VAERS receives approximately 12,000 reports annually, and since 1991 has received at least 75,000 reports. However, VAERS solicits reports of events not only known to be causally relat-

ed to vaccine but all events temporally related to immunization, a portion of which may be coincidental. Data collected on the VAERS form include age, sex, birth weight (in patients younger than 6 years), date of vaccination, type of vaccine, manufacturer, lot number, number of previous doses of vaccine, date of onset of symptoms, and clinical description of the event (Figure 1). Events are classified by severity: death, serious (Table 3), and non-serious. About 15% of reports describe serious events, and 85% are non-serious. An “unexpected” event is an event not noted in the FDA-approved manufacturers’ labeling of the vaccine. All reports of deaths and serious events received by the FDA are followed-up by telephone and/or written inquiry by FDA staff or VAERS contractor. Letters to follow-up serious reports and obtain the recovery status are mailed to the reporters at 60 days and 1 year after vaccination. The signs, symptoms, and diagnoses mentioned in the narrative description of the adverse event is coded using FDA’s Coding Symbols for Thesaurus of Adverse Reaction Terms (COSTART). All information obtained from the original and follow-up VAERS report is entered as computerized data and stored in a relational database for subsequent analysis.

The VAERS database, excluding patient identifiers, is available to the public from the National Technical Information Service (NTIS), telephone: (703) 487-4650, or Freedom of Information (FOI) staff can respond to requests for portions of the database or redacted copies of VAERS forms, telephone: (301) 827-2000. [General information and the VAERS form itself are available on the VAERS Internet website:](http://www.fda.gov/cber/vaers.html)

<http://www.fda.gov/cber/vaers.html>.

Based on careful review of spontaneous reports, FDA can initiate various actions: manufacturers’ labeling or packaging change(s), conducting or requesting manufacturer-sponsored post-marketing epidemiologic investigations (hypotheses testing in more rigorous databases) (2,3,11), issuing a Safety Alert or “Dear Health Professional” letter, inspecting manufacturers’ facilities/records, or working with a manufacturer regarding possi-

ble withdrawal of vaccine from the market (for safety or efficacy reasons). Keeping vaccine labeling/package inserts up-to-date is an ongoing, dynamic process that depends on new information gleaned from spontaneous adverse event reports.

Dissemination of safety-related information to health care professionals and the public is an important public health goal of post-marketing surveillance.

### OBJECTIVES OF VAERS AND RESULTS OF ANALYSES OF VAERS DATA

#### *Identification of new, rare vaccine reactions, increased rates of known side effects, risk factors for adverse events*

Several investigations based on VAERS data have uncovered previously unrecognized problems that may occur in vaccine recipients, including: rare life-threatening thrombocytopenia after measles-mumps-rubella (MMR) vaccination (Box 1) (4), hair loss after hepatitis B vaccination (Box 2) (5), serious injuries resulting from vaccine-induced syncope or fainting (Box 3) (6), and identification of the low risk of convulsions following receipt of DTP and measles-containing vaccines (10). VAERS can also be used to evaluate the safety of vaccinating a new sub-group of the population (e.g., universal immunization of infants with hepatitis B vaccine

TABLE 3

#### FDA CLASSIFICATION OF SERIOUS VAERS EVENT:

*An event with one of the following patient outcomes:*

1. Fatal
2. Life-threatening
3. Persistent or significant disability/incapacity
4. Requires or prolongs hospitalization
5. Congenital anomaly/birth defect
6. Requires intervention to prevent an outcome listed above



after the vaccine had been initially used in adult health care workers)(7), assessing the safety of newly licensed vaccines (e.g., hepatitis A [8], varicella [FDA, unpublished data], DTaP [10]), or comparing the safety of two brands of vaccine (9).

### ***Identification of vaccine lots with increased numbers of types of reported events***

Since 1993, FDA staff have performed weekly review of the numbers and types of reported events in specific vaccine lots based on distribution data provided by vaccine manufacturers (proprietary data). Evaluating lot-specific reports is problematic as vaccine lot size greatly varies (range: 3,000-700,000 doses), and more reports are usually received for a large lot than a small one. To date, no lot has been found to be unsafe. This result is not surprising given the stringency of the manufacturing and testing requirements to which vaccines are subject. Nevertheless, because of the possibility of such a problem arising, regular attention to lot-specific reports is an important aspect of FDA's program of vaccine safety monitoring.

There have only been four FDA-initiated recall of vaccines since 1987: One lot was recalled after FDA detected particulates, another lot was mislabeled, the third was recalled because of violations in manufacturing practices at a production plant that was found after an FDA inspection, and the fourth was because of a decrease in vaccine potency over time.

### **POST-MARKETING REPORTING OF ADVERSE EVENTS: THE CRITICAL ROLE OF HEALTH PROFESSIONALS**

The FDA has the regulatory responsibility to ensure the safety of vaccines. Determination of whether an event was caused by the vaccine is not a pre-requisite for filing a VAERS report. VAERS solicits reports for all events temporally related to vaccination, some of which may be coincidental (1-3). Any index of suspicion that a serious event or death may be related to vaccination is reason for the health professional to submit a VAERS report. The role of the health professional in supporting the national passive surveil-

lance system is essential, as the first hint of a potential problem usually originates with the astute clinician who reported the case to the appropriate source. Post-marketing surveillance relies on health professionals to report suspicious events, thus improving the quality of reported data, and contributing significantly to safeguarding public health in vaccine safety.

#### **BOX 1: SEVERE THROMBOCYTOPENIA AFTER MMR II IMMUNIZATION (4)**

A cluster of VAERS reports of severe thrombocytopenia (TP) after MMR II immunization prompted FDA review. 55 reports coded thrombocytopenia or thrombocytopenia purpura were retrieved from 8,581 reports for measles-containing vaccines. 55% occurred in children < 2 years old (range 1-40 years) and cases were evenly distributed between males and females. 42 reports noted onset of symptoms 3 to 32 days after vaccination (median time to diagnosis, 12 days), 41 cases necessitated hospitalization, 17 patients were treated with intravenous immunoglobulin and/or steroids and one 12 year-old male had splenectomy.

Two serious complications were reported: a 1 year-old male (platelet count, 1,000/mm<sup>3</sup>, 12 days after immunization) had severe gastrointestinal hemorrhage requiring blood transfusions; a 15 month-old male (platelet count, 5,000/mm<sup>3</sup>,) had pulmonary hemorrhage. There were 2 deaths: a 17 year-old male with history of recurrent TP secondary to antiphospholipid syndrome died from sepsis 4 days after immunization; a 4 year-old male died 7 days after receiving vaccine from *Escherichia coli* 0157:H7 infection complicated by pseudomembranous colitis.

Platelet counts reported for 42 persons ranged from 1,000 to 102,000 mm<sup>3</sup>; 29 had platelet counts ≤20,000/mm<sup>3</sup>. These findings suggest that individuals with a history of TP, regardless of etiology, may have recurrent episodes of TP after immunization, and deserve a careful risk-benefit analysis before receiving vaccine. These reports represent 0.07% of reports for measles-containing vaccines received by VAERS, and suggest that post-vaccination TP is a rare event.

#### **BOX 2:**

#### **HAIR LOSS AFTER IMMUNIZATION (5)**

One day after a 30 year-old female nurse's first dose of hepatitis B (HepB) vaccine, she developed mild hair loss, arthralgias, fatigue and weakness which lasted 1 week. One day after her second HepB dose she had recurrent hair loss, and 2 weeks later, recurrent arthralgias, fatigue and weakness. Alopecia progressed for a few months until approximately half of her hair had a diffuse, thinned appearance. Her hair later regrew without treatment or workup.

#### **BOX 3:**

#### **SYNCOPE AFTER IMMUNIZATION (6)**

697 cases of syncope after vaccination were reported. 77.4% were younger than 20 years, and 57.5% were female. Hospitalization was reported in 9.6%. Of the 571 syncope events with known interval to onset, 511 occurred 1 hour or less after vaccination, and 323 (63.2%) occurred within the first 5 minutes after vaccination. Tonic or clonic movements were reported in 30.4% of syncopal episodes occurring 15 minutes less, and in 12.8% of those occurring 15 minutes or longer after vaccination ( $p < 0.01$ ).

Six patients suffered skull fracture, cerebral bleeding or cerebral contusion after falls; 3 of these patients required neurosurgery. Falls occurred 15 minutes or less after vaccination in or near the clinic or office. Ages ranged from 12 to 28 years; 5 of 6 were male. Follow-up revealed substantial residual impairment in 2 patients.

Prevention of injury from syncope after vaccination may be possible. Vaccinators should be aware that patients exhibiting pre-syncopal signs and symptoms (hypotension, bradycardia, anxiety, pallor, cool clammy skin) around the time of immunization may need to be seated or lie down after immunization until free of symptoms.



## FDA EVALUATION OF REPORTS OF ADVERSE EVENTS

The uncontrolled nature of spontaneously reported data places great importance on the evaluation of submitted reports of adverse events. These analyses, applied on a case-by-case basis, are based on experience and knowledge of the vaccine being monitored and awareness of the limitations of the data. A major objective of the national VAERS is to disseminate vaccine safety information based on these analyses to the scientific community and the public through publications and presentation (2-16).

## COMPARISON OF VAERS AND MEDWATCH SURVEILLANCE SYSTEMS

FDA maintains two national passive surveillance systems monitoring the post-marketing safety of medicinal products: VAERS and MEDWATCH (a system which monitors the safety of medical products and devices that are not vaccines). Both systems mandate that manufacturers, distributors, pharmaceutical packers, and device user facilities of FDA-approved medical products report adverse events according to specific reporting requirements (Table 2).

## SUMMARY

The effectiveness of a national post-marketing surveillance program is directly dependent on the active participation of health professionals. Despite the limitations of spontaneous reports, FDA's program for vaccine surveillance provides vital information of clinical importance. The identification of signals in adverse event surveillance may initiate further investigation of potential problems in vaccine safety or efficacy, and the subsequent dissemination of safety-related information to the scientific community and the public. **This process begins with and is dependent upon voluntary submission of reports of possible vaccine-associated events to VAERS by the astute, conscientious health professional.**

TABLE 4

### HOW TO OBTAIN VAERS FORMS AND INSTRUCTIONS

**Copies of VAERS form (Figure 1) can be obtained from:**

VAERS  
P.O. Box 1100  
Rockville, Maryland 29849-1100

**Copies of VAERS form and instructions may also be obtained by:**

- Mail: Call 800-822-7967 or FAX request to: 877-721-0366
- If no access to 800 number: Call (301) 562-1086
- Internet: Visit the VAERS Website at [www.vaers.org](http://www.vaers.org)

**Where to send VAERS forms:**

VAERS  
P.O. Box 1100  
Rockville, Maryland 29849-1100

**Questions about reporting?**

Epidemiology Branch, ATTN: VAERS  
Center for Biologics Evaluation and Research  
U.S. Food and Drug Administration  
1401 Rockville Pike, HFM-210  
Rockville, Maryland 20852-1448  
Phone: (301) 827-3974  
FAX: (301) 827-3529

## VAERS

### Vaccine Adverse Event Reporting System

*A Cooperative Program of the Centers for Disease Control and Prevention and the Food and Drug Administration*

**Call 1-800-822-7967 for VAERS Reporting Information**



VAERS  
P.O. Box 1100  
Rockville, MD 20849-1100  
FAX: (877) 721-0366

**VAERS E-mail: [info@vaers.org](mailto:info@vaers.org) Web: [www.vaers.org](http://www.vaers.org)**

**CDC NP Website**  
**<http://www.cdc.gov/nip>**

**FDA CBER Website**  
**<http://www.fda.gov/cber>**

Figure 1: VAERS Form

 <b>VACCINE ADVERSE EVENT REPORTING SYSTEM</b> 24 Hour Toll-free information line 1-800-822-7967 P.O. Box 1100, Rockville, MD 20849-1100 <b>PATIENT IDENTITY KEPT CONFIDENTIAL</b>				For CDC/FDA Use Only	
<b>Patient Name:</b> Last _____ First _____ M.I. _____ Address _____ _____ _____ City _____ State _____ Zip _____ Telephone no. (____) _____				<b>Vaccine administered by (Name):</b> _____ <b>Responsible Physician:</b> _____ <b>Facility Name/Address:</b> _____ _____ _____ City _____ State _____ Zip _____ Telephone no. (____) _____	
<b>Form completed by (Name):</b> _____ <b>Relation to Patient:</b> Vaccine Provider _____ Patient/Parent _____ Manufacturer _____ Other _____ <b>Address (if different from patient or provider):</b> _____ _____ _____ City _____ State _____ Zip _____ Telephone no. (____) _____				<b>VAERS Number:</b> _____ <b>Date Received:</b> _____	
1. State	2. County where administered	3. Date of birth mm / dd / yy	4. Patient age mm / dd / yy	5. Sex M F	6. Date form completed mm / dd / yy
7. Describe adverse event(s) (symptoms, signs, time course) and treatment, if any: _____ _____ _____				8. Check all appropriate: <input type="checkbox"/> Patient died (date mm / dd / yy) <input type="checkbox"/> Life threatening illness <input type="checkbox"/> Required emergency room/doctor visit <input type="checkbox"/> Required hospitalization (____ days) <input type="checkbox"/> Resulted in prolongation of hospitalization <input type="checkbox"/> Resulted in permanent disability <input type="checkbox"/> None of the above	
9. Patient recovered: YES NO UNKNOWN				10. Date of vaccination mm / dd / yy AM PM	11. Adverse event onset mm / dd / yy AM PM
12. Relevant diagnostic tests/laboratory data: _____					
13. Enter all vaccines given on date listed in no. 10					
Vaccine (type)		Manufacturer	Lot number	Route/Site	No. Previous doses
a. _____		_____	_____	_____	_____
b. _____		_____	_____	_____	_____
c. _____		_____	_____	_____	_____
d. _____		_____	_____	_____	_____
14. Any other vaccinations within 4 weeks prior to the date listed in no. 10					
Vaccine (type)		Manufacturer	Lot number	Route/Site	No. Previous doses
a. _____		_____	_____	_____	_____
b. _____		_____	_____	_____	_____
c. _____		_____	_____	_____	_____
d. _____		_____	_____	_____	_____
15. Vaccinated at: Private doctor's office/hospital Public health clinic/hospital		16. Vaccine purchased with: Military clinic/hospital Other/unknown		17. Other medications	
18. Illness at time of vaccination (specify)		19. Pre-existing physician-diagnosed allergies, birth defects, medical conditions (specify)			
20. Have you reported this adverse event previously? No To health department To doctor To manufacturer		<b>Only for children 5 and under</b> 22. Birth weight lb. ____ oz. ____ 23. No. of brothers and sisters _____			
21. Adverse event following prior vaccination (check all that apply, specify)		<b>Only for reports submitted by manufacturer/immunization project</b> 24. Mfr./imm. proj. report no. _____ 25. Date received by mfr./imm. proj. _____			
Adverse Event Onset Age Type Dose no. in series In patient _____ In teacher _____ on sister _____		26. 15-day report? Yes No 27. Report type Initial Follow-Up			
<small>Health care providers and manufacturers are required by law (42 USC 300aa-25) to report reactions to vaccines listed in the Table of Reportable Events Following Immunization. Reports for reactions to other vaccines are voluntarily accepted when required as a condition of immunization grant awards.</small>					



"Fold in thirds, tape & mail - DO NOT STAPLE FORM"



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**VAERS**

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Rockville, MD 20849-1800



### DIRECTIONS FOR COMPLETING FORM

(Additional pages may be attached if more space is needed.)

#### GENERAL

- Use a separate form for each patient. Complete the form to the best of your abilities. Items 3, 4, 7, 8, 10, 11, and 13 are considered essential and should be completed whenever possible. Parents/Guardians may need to consult the facility where the vaccine was administered for some of the information (such as manufacturer, lot number or laboratory data.)
- Refer to the Reportable Events Table (RET) for events mandated for reporting by law. Reporting for other serious events felt to be related but not on the RET is encouraged.
- Health care providers other than the vaccine administrator (VA) treating a patient for a suspected adverse event should notify the VA and provide the information about the adverse event to allow the VA to complete the form to meet the VA's legal responsibility.
- These data will be used to increase understanding of adverse events following vaccination and will become part of CDC Privacy Act System 09-20-0138, "Epidemiologic Studies and Surveillance of Disease Problems". Information identifying the person who received the vaccine or that person's legal representative will not be made available to the public, but may be available to the vaccinee or legal representative.
- Postage will be paid by addressee. Forms may be photocopied (must be front & back on same sheet).

#### SPECIFIC INSTRUCTIONS

**Form Completed By:** To be used by parents/guardians, vaccine manufacturers/distributors, vaccine administrators, and/or the person completing the form on behalf of the patient or the health professional who administered the vaccine.

- Item 7:** Describe the suspected adverse event. Such things as temperature, local and general signs and symptoms, time course, duration of symptoms, diagnosis, treatment and recovery should be noted.
- Item 9:** Check "YES" if the patient's health condition is the same as it was prior to the vaccine, "NO" if the patient has not returned to the pre-vaccination state of health, or "UNKNOWN" if the patient's condition is not known.
- Item 10:** Give dates and times as specifically as you can remember. If you do not know the exact time, please
- and 11:** indicate "AM" or "PM" when possible if this information is known. If more than one adverse event, give the onset date and time for the most serious event.
- Item 12:** Include "negative" or "normal" results of any relevant tests performed as well as abnormal findings.
- Item 13:** List ONLY those vaccines given on the day listed in Item 10.
- Item 14:** List any other vaccines that the patient received within 4 weeks prior to the date listed in Item 10.
- Item 15:** This section refers to how the person who gave the vaccine purchased it, not to the patient's insurance.
- Item 17:** List any prescription or non-prescription medications the patient was taking when the vaccine(s) was given.
- Item 18:** List any short term illnesses the patient had on the date the vaccine(s) was given (i.e., cold, flu, ear infection).
- Item 19:** List any pre-existing physician diagnosed allergies, birth defects, medical conditions (including developmental and/or neurologic disorders) for the patient.
- Item 21:** List any suspected adverse events the patient, or the patient's brothers or sisters, may have had to previous vaccinations. If more than one brother or sister, or if the patient has reacted to more than one prior vaccine, use additional pages to explain completely. For the onset age of a patient, provide the age in months if less than two years old.
- Item 26:** This space is for manufacturers' use only.

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## CONTINUING MEDICAL EDUCATION (CME) QUESTIONS &amp; ANSWERS

**1. Which of the following is NOT a known limitation of pre-marketing clinical trials?**

- A. Ability to detect common adverse reactions.
- B. Small study size.
- C. Short study duration.
- D. Narrow set of indications.
- E. Evaluates diverse populations.

**2. Which of the following statements is TRUE?**

- A. Post-marketing passive surveillance is conducted under controlled conditions in defined populations.
- B. The ability to detect adverse events after vaccination is enhanced with the routine use of multiple vaccines.
- C. Adverse event detection relies on accurate reporting from health care providers.
- D. The number of doses of vaccine administered to the public is accessible to the public.
- E. Once a vaccine is marketed, its initial/product information does not change.

**3. All of the following are known limitations of passive surveillance systems based on spontaneous reports EXCEPT:**

- A. Includes the entire U.S. population.
- B. Under-reporting.
- C. Bias.
- D. Lack of consistent diagnostic criteria for disease.
- E. Lack of denominator data.

**4. All of the following are known strengths of spontaneous (passive) surveillance systems based on spontaneous reports EXCEPT:**

- A. Cost-effective in detecting rare, serious adverse events.
- B. Hypothesis generation (identification of a signal).
- C. Studies geographically diverse population.
- D. Relatively immune to bias.
- E. Large portion of voluntary reports from conscientious, astute health professionals.

**5. Which of the following statements is FALSE with regard to VAERS?**

- A. An event that is life-threatening or requires hospitalization or prolonged hospitalization, or permanent disability is considered serious.
- B. An event must be causally related to vaccine to be reported to VAERS.
- C. VAERS can assess the safety of specific vaccine lots.
- D. Manufacturers are required to report serious adverse events to VAERS.
- E. The identity of the vaccinee is kept confidential.

**6. Objectives of VAERS includes all of the following EXCEPT:**

- A. Identification of increased rates of known side effects.
- B. Identification of risk factor that may promote disease.
- C. Identification of new, rare vaccine reactions.
- D. Assessment of vaccine lot safety.
- E. Conduct of controlled studies to determine if an event was caused by the vaccine.

**7. Which of the following is FALSE?**

- A. Careful consideration of the limitations of VAERS is relevant to accurate interpretation of VAERS data.
- B. A large number of VAERS events cannot be interpreted as clear-cut evidence that an event is causally related to vaccination.
- C. Biological plausibility and strength of association are very important in adverse event report evaluation.
- D. It is possible to interpret VAERS data without knowing the number of persons who were vaccinated ("denominator" data).
- E. Follow-up epidemiologic investigations may stem from identification of unusual VAERS reports.

**8. All of the following are FDA actions that can result from careful analysis of spontaneous adverse event reports EXCEPT:**

- A. Requesting manufacturer-sponsored post-marketing studies.
- B. Requiring manufacturer to compensate for damages suffered because of a vaccine-related adverse event.
- C. Change in label/product information.
- D. Working with manufacturer on the issuance of a Safety Alert that outlines the serious safety issue involved.
- E. Recalling a vaccine lot.

**9. All of the following are methods by which the FDA disseminates vaccine safety-related information to health care providers EXCEPT:**

- A. Publications in scientific literature.
- B. Presentations at public forums.
- C. VAERS Website on the internet.
- D. Work with manufacturers on the issuance of "Dear Health Professional" letters.
- E. None of the above -- ALL are used by the FDA to inform health care providers of new safety information.

**10. The effectiveness of VAERS is dependent on all of the following EXCEPT:**

- A. Active participation of health professionals to report vaccine-associated events to VAERS.
- B. Adequately financing the high costs needed to maintain VAERS.
- C. Careful consideration of the limitations of VAERS while interpreting data.
- D. Ensuring confidentiality against disclosure of patient identifies.
- E. Filing of complete VAERS reports including clinical diagnosis and details of the course of events.

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PUBLICATION DATE: OCTOBER 31, 1998

NOTE: THIS PROGRAM EXPIRES ON OCTOBER 31, 2001

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 Please cut along dotted line

Post-Marketing Surveillance: VAERS

# MEDWATCH

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1. \_\_\_\_\_ 2. \_\_\_\_\_ 3. \_\_\_\_\_ 4. \_\_\_\_\_ 5. \_\_\_\_\_ 6. \_\_\_\_\_ 7. \_\_\_\_\_ 8. \_\_\_\_\_ 9. \_\_\_\_\_ 10. \_\_\_\_\_

Date: \_\_\_\_\_ Phone Number: \_\_\_\_\_

Name (including degree): \_\_\_\_\_

Professional Specialty: \_\_\_\_\_

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Amount of time spent completing this CE program: \_\_\_\_\_ hours (must be completed for CME credit)

The information presented is relevant to my clinical practice \_\_\_\_\_ Y \_\_\_\_\_ N

1. Was the material new for you? \_\_\_\_\_ Y \_\_\_\_\_ N

2. Was the material presented clearly? \_\_\_\_\_ Y \_\_\_\_\_ N

3. Was the material covered adequately? \_\_\_\_\_ Y \_\_\_\_\_ N

4. Can you explain the importance of vaccine post-marketing surveillance? \_\_\_\_\_ Y \_\_\_\_\_ N

5. Are you able to define your responsibility to report adverse events? \_\_\_\_\_ Y \_\_\_\_\_ N

6. Are you able to discuss basic limitations and strengths of VAERS? \_\_\_\_\_ Y \_\_\_\_\_ N

7. Do you understand the objectives of VAERS? \_\_\_\_\_ Y \_\_\_\_\_ N

8. Are you able to describe ways in which FDA informs health professionals about vaccine safety? \_\_\_\_\_ Y \_\_\_\_\_ N

9. Are you able to describe what impact post-marketing passive surveillance systems have on your clinical practice? \_\_\_\_\_ Y \_\_\_\_\_ N

10. Would you like to see more CE courses from FDA? \_\_\_\_\_ Y \_\_\_\_\_ N

Suggested Topics: \_\_\_\_\_

Mail the completed answer sheet by 10/31/01 to:

FDA/CBER/DBE, 1401 Rockville Pike, HFM-210, Rockville, MD 20852 or FAX it to (301) 827-3529  
or submit your answers online ([www.fda.gov/medwatch](http://www.fda.gov/medwatch))



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**VAERS**

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**THE FDA/CDC VACCINE ADVERSE  
EVENT REPORTING SYSTEM**

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[www.fda.gov/cber/vaers.html](http://www.fda.gov/cber/vaers.html)

**Post-marketing surveillance for adverse events after vaccination:  
the national Vaccine Adverse Event Reporting System (VAERS)**

Complimentary CE Article





**To:** Françoise Sillan, Corinne  
Jouquelet-Royer

**From:** Anne-Céline Eydan

Request date: July 8, 2014

Delivery date: July 23, 2014

**Subject: Safety surveillance: Observational Studies**

Search strategy

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#5	'vaccine'/exp/dd_ae
#1	'observational study'/exp

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## Low & Middle Income Countries

### **Children who received PCV-10 vaccine from a two-dose vial without preservative are not more likely to develop injection site abscess compared with those who received pentavalent (DPT-HepB-Hib) vaccine: A longitudinal multi-site study**

[Berhane Y.](#), [Worku A.](#), [Demissie M.](#), [Tesfaye N.](#), [Asefa N.](#), [Aniemaw W.](#), [Weldearegawi B.](#), [Kebede Y.](#), [Shiferaw T.](#), [Worku A.](#), [Olijira L.](#), [Merdekios B.](#), [Ashebir Y.](#), [Tadesse T.](#), [Dessie Y.](#), [Meseret S.](#), [Ayele G.](#)

PLoS ONE 2014 9:6 Article Number e97376

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**Background:** The single dose pneumonia ten-valent vaccine has been widely used and is highly efficacious against selected strains *Streptococcus pneumoniae*. A two-dose vial without preservative is being introduced in developing countries to reduce the cost of the vaccine. In routine settings improper immunization practice could result in microbial contamination leading to adverse events following immunization. **Objective:** To monitor adverse events following immunization recommended for routine administration during infancy by comparing the rate of injection-site abscess between children who received PCV-10 vaccine and children who received the Pentavalent (DPT-HepB-Hib) vaccine. **Methods:** A longitudinal population-based multi-site observational study was conducted between September 2011 and October 2012. The study was conducted in four existing Health and Demographic Surveillance sites run by public universities of Abraminch, Haramaya, Gondar and Mekelle. Adverse events following Immunization were monitored by trained data collectors. Children were identified at the time of vaccination and followed at home at 48 hour and 7 day following immunization. Incidence of abscess and relative risk with the corresponding 95% Confidence Intervals were calculated to examine the risk



difference in the comparison groups. Results: A total of 55, 268 PCV and 37, 480 Pentavalent (DPT-HepB-Hib) vaccinations were observed. A total of 19 adverse events following immunization, 10 abscesses and 9 deaths, were observed during the one year study period. The risk of developing abscess was not statistically different between children who received PCV-10 vaccine and those received Pentavalent (RR = 2.7, 95% CI 0.576-12.770), and between children who received the first aliquot of PCV and those received the second aliquot of PCV (RR = 1.72, 95% CI 0.485-6.091). Conclusion: No significant increase in the risk of injection site abscess was observed between the injection sites of PCV-10 vaccine from a two-dose vial without preservative and pentavalent (DPT-HepB-Hib) vaccine in the first 7 days following vaccination. © 2014 Berhane et al.

**A prospective observational safety study on MF59® adjuvanted cell culture-derived vaccine, Celtura® during the A/H1N1 (2009) influenza pandemic**

[Reynales H.](#), [Astudillo P.](#), [de Vallière S.](#), [Hatz C.](#), [Schlagenhauf P.](#), [Rath B.](#), [Velentgas P.](#), [Fariña A.](#), [Sales-Carmona V.](#), [Groth N.](#)

**Vaccine** 2012 **30:45** (6436-6443)

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Background: The present study was a prospective observational study to evaluate the safety profile of Celtura®, a monovalent, cell culture-derived, inactivated subunit influenza vaccine prepared from A/California/07/2009(H1N1) with the adjuvant MF59®. Subjects were enrolled prospectively during the H1N1 2009 influenza pandemic at medical centres in **Colombia, Chile, Switzerland, and Germany** during the period December 2009 to June 2010. Methods: Subjects ages 18 and older were followed for the occurrence of adverse events (AEs) for six months after vaccination. Adverse events of special interest (AESIs) were neuritis, convulsion (seizure), anaphylaxis, encephalitis, vasculitis, Guillain-Barre syndrome, demyelinating conditions, Bell's palsy, and laboratory-confirmed vaccination failure. Results: Overall, 7348 AEs were reported in 2296 of 3989 enrolled subjects (57.6%). Only two AEs were considered related to injection site reactions. No laboratory-confirmed cases of influenza were reported. There were 108 medically confirmed serious adverse events (SAEs) reported among 73 subjects with 6 such SAEs described as possibly or probably related to vaccination. Three fatal cases were reported and assessed as not related to vaccination. Two AESIs classified as convulsion were reported and assessed as not related to vaccination. Both AESIs occurred well outside the pre-specified 7 day risk window representing the likely timeframe of the occurrence of seizure following vaccination. Conclusions: The results of this study support the overall good safety profile of MF59 adjuvanted cell culture-derived influenza vaccine as administered in adults during the 2009-2010 H1N1 influenza pandemic. No concern is raised regarding the occurrence of AESIs. © 2012 Elsevier Ltd.

**Safety observation of influenza a H1N1 influenza vaccine vaccinations in 3300 medical workers**

[He X.-L.](#), [Kang S.-Q.](#), [Gong C.-Y.](#), [Jiang G.-Y.](#)



Objective: To investigate safety of influenza A H1N1 vaccine vaccinations.

Methods: A total of 3 300 medical workers were vaccinated by batch of 200909012 influenza A H1N1 vaccine produced by Shanghai Biological Products Corporation Limited according to the principle of voluntary and concentration. The adverse reactions were observed within half an hour, three days and a week after vaccinations, respectively. Results: The inoculators with local or systemic reaction reached 1.18% (39/3 300). There were 0.15% (5/3 300) of the inoculators with adverse reaction within half an hour; 0.70% (23/3 300) within 1 to 3 days after vaccination; and 0.33% (11/3 300) within 3 days to 1 week after vaccination. No severe adverse events were found. Conclusion: Influenza A H1N1 vaccine vaccinations is an economic and effective way of influenza A H1N1 prevention with mild reactions. © 2010 Editorial Board of Chin J Evid-based Med.

### **Active assessment of adverse events following yellow fever vaccination of persons aged 60 years and more**

[Miyaji K.T.](#), [Luiz A.M.](#), [Lara A.N.](#), [Chaves T.D.S.S.](#), [Piorelli R.D.O.](#), [Lopes M.H.](#), [Sartori A.M.C.](#)

**Human Vaccines and Immunotherapeutics** 2013 **9:2** (277-282)

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Introduction: Older age has been associated to serious adverse events (AE) following yellow fever (YF) vaccination in passive surveillance studies, but few prospective studies involving seniors have been published. Results: Nine hundred and six persons were evaluated; 78 were not vaccinated and 828 received the vaccine; 700 (84.7%) were interviewed after vaccination: 593 (84.7%) did not report any symptoms or signs following YF vaccine; 107 (15.3%) reported at least one AE temporally associated to YF vaccination: 97 (13.9%) had systemic AE and 17 (2.4%) reported AE at the injection site (7 had both systemic and local AE). Data regarding previous vaccination was available for 655 subjects. Statistically significant higher rates of systemic AE were observed among subjects who received the first YF vaccination (17.5%) in comparison to persons who had been previously vaccinated (9.5%). Methods: This observational prospective study aimed to describe AE following YF vaccination in persons aged  $\geq 60$  y. From March 2009 to April 2010, seniors who sought YF vaccination at a reference Immunization Center in **Sao Paulo city, c Brazil**, were included. Demographic and clinical data, previous YF vaccination, travel destination and the final decision regarding YF vaccination or not were collected from standardized medical records. Active AE assessment was done through telephone or electronic mail interview performed approximately 14 d after immunization. Conclusion: Most persons aged  $\geq 60$  y may be safely vaccinated against YF. Before vaccination, they must be carefully screened for conditions associated to altered immunocompetence and for risk of exposure to YF. © 2013 Landes Bioscience.



## Long-term follow-up observation of the safety, immunogenicity, and effectiveness of Gardasil™ in adult women

[Luna J.](#), [Plata M.](#), [Gonzalez M.](#), [Correa A.](#), [Maldonado I.](#), [Nossa C.](#), [Radley D.](#), [Vuocolo S.](#), [Haupt R.M.](#), [Saah A.](#)

**PLoS ONE** 2013 **8:12** Article Number e83431

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Background: Previous analyses from a randomized trial in women aged 24-45 have shown the quadrivalent HPV vaccine to be efficacious in the prevention of infection, cervical intraepithelial neoplasia (CIN) and external genital lesions (EGL) related to HPV 6/11/16/18 through 4 years. In this report we present long term follow-up data on the efficacy, safety and immunogenicity of the quadrivalent HPV vaccine in adult women. Methods: Follow-up data are from a study being conducted in 5 sites in **Colombia** designed to evaluate the long-term immunogenicity, effectiveness, and safety of the qHPV vaccine in women who were vaccinated at 24 to 45 years of age (in the original vaccine group during the base study [n = 684]) or 29 to 50 years of age (in the original placebo group during the base study [n = 651]). This analysis summarizes data collected as of the year 6 post-vaccination visit relative to day 1 of the base study (median follow-up of 6.26 years) from both the original base study and the Colombian follow-up. Results: There were no cases of HPV 6/11/16/18-related CIN or EGL during the extended follow-up phase in the per-protocol population. Immunogenicity persists against vaccine-related HPV types, and no evidence of HPV type replacement has been observed. No new serious adverse experiences have been reported. Conclusions: Vaccination with qHPV vaccine provides generally safe and effective protection from HPV 6-, 11-, 16-, and 18-related genital warts and cervical dysplasia through 6 years following administration to 24-45 year-old women. Trial Registration: Clinicaltrials.gov NCT00090220 © 2013 Luna et al.

## Post-authorization safety surveillance of a liquid pentavalent vaccine in Guatemalan children

[Asturias E.J.](#), [Contreras-Roldan I.L.](#), [Ram M.](#), [Garcia-Melgar A.J.](#), [Morales-Oquendo V.](#), [Hartman K.](#), [Rauscher M.](#), [Moulton L.H.](#), [Halsey N.A.](#)

**Vaccine** 2013 **31:49** (5909-5914)

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Objective: Combination vaccines have improved the efficiency of delivery of new vaccines in low and middle-income countries. Post-authorization monitoring of adverse events (AEs) after vaccination with a liquid pentavalent DTwP-HepB-Hib combination vaccine was conducted in Guatemalan infants. Methods: A prospective observational safety study of the incidence of medical attended events (MAEs) and serious adverse events (SAEs) in children who received pentavalent and oral polio vaccines at 2, 4 and 6 months of age was conducted in two clinics at the Institute of Guatemala. Parents were contacted by telephone after each dose. All outpatient, emergency department visits, and hospitalizations were monitored. A self-controlled analysis was conducted to determine if there was evidence of increased risk of MAEs or SAEs following vaccines as compared to control time windows. Results: Of 3000 recruited infants, 2812 (93.7%) completed the third dose and 2805 (93.5%) completed follow-up. Ten AEs in eight infants, of which four SAEs in four infants, were classified as related to the vaccine. Thirteen deaths were reported due to



common illnesses of infancy, and none were judged to be related to the vaccine. The mortality rate (4.4 per 1000) was lower than expected for the population. The incidence-rate-ratio for healthcare visits was lower in post-vaccination time windows than for control windows; after the first vaccine dose, the rate ratios for the risk periods of 0-1, 2-6, and 7-30 days post-vaccination were 0.3, 0.5, and 0.7, respectively (all statistically significantly different from the reference value of 1.0 for the 31-60 day control period). Conclusion: The liquid pentavalent vaccine was associated with lower rates of health care visits and not associated with increases in SAEs or hospitalizations. Systems can be set up in low to middle income countries to capture all health care visits to monitor the safety of new vaccines. © 2013 Elsevier Ltd.

### **Long-term follow-up of study participants from prophylactic HIV vaccine clinical trials in Africa**

[Schmidt C.](#), [Jaoko W.](#), [Omosa-Manyonyi G.](#), [Kaleebu P.](#), [Mpendo J.](#), [Nanvubya A.](#), [Karita E.](#), [Bayingana R.](#), [Bekker L.-G.](#), [Chomba E.](#), [Kilembe W.](#), [Nchabeleng M.](#), [Nyombayire J.](#), [Stevens G.](#), [Chetty P.](#), [Lehrman J.](#), [Cox J.](#), [Allen S.](#), [Dally L.](#), [Smith C.](#), [Fast P.E.](#)

**Human Vaccines and Immunotherapeutics** 2014 **10:3** (714-723)

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Long-term safety is critical for the development and later use of a vaccine to prevent HIV/AIDS. Likewise, the persistence of vaccine-induced antibodies and their impact on HIV testing must be established. IAVI has sponsored several Phase I and IIA HIV vaccine trials enrolling healthy, HIV-seronegative African volunteers. Plasmid DNA and viral vector based vaccines were tested. No vaccine-related serious adverse events were reported. After completion of vaccine trials conducted between 2001-2007, both vaccine and placebo recipients were offered enrolment into an observational long-term follow-up study (LTFU) to monitor potential late health effects and persistence of immune responses. At scheduled 6-monthly clinic visits, a health questionnaire was administered; clinical events were recorded and graded for severity. Blood was drawn for HIV testing and cellular immune assays. 287 volunteers were enrolled; total follow-up after last vaccination was 1463 person years (median: 5.2 years). Ninety-three (93)% of volunteers reported good health at their last LTFU visit. Infectious diseases and injuries accounted for almost 50% of the 175 reported clinical events, of which over 95% were mild or moderate in severity. There were 30 six pregnancies, six incident HIV infections and 14 volunteers reported cases of social harm. Persistence of immune responses was rare. No safety signal was identified. No potentially vaccine-related medical condition, no immune mediated disease, or malignancy was reported. HIV vaccines studied in these trials had a low potential of induction of persisting HIV antibodies. © 2014 Landes Bioscience.

### **Other countries**



## **Prospective safety monitoring of Haemophilus influenzae type b and heptavalent pneumococcal conjugate vaccines in Kagoshima, Japan**

[Nishi J.](#), [Tokuda K.](#), [Imuta N.](#), [Minami T.](#), [Kawano Y.](#)

**Japanese Journal of Infectious Diseases** 2013 **66:3** (235-237)

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Haemophilus influenzae type b (Hib) conjugate vaccine (PRP-T) and heptavalent pneumococcal conjugate vaccine (PCV7) were introduced in Japan in December 2008 and February 2010, respectively. The concurrent administration of these vaccines is routinely performed worldwide. However, the safety of the simultaneous administration of these vaccines has not been fully evaluated in Japan, because it has rarely been performed thus far. We conducted a 2-year prospective, observational, multicenter study on PRP-T and PCV7 safety from February 2009 through January 2011 in 29 facilities located in Kagoshima Prefecture, Japan. Objective severe adverse events included anaphylactoid reaction, encephalitis/encephalopathy, neurological events, severe focal reactions, systemic eruption/urticaria, fever above 39.9°C within 2 days after inoculation, and other complications requiring hospitalization. The incidences of these events for PRP-T and PCV7 administration were 0.68% (76/11,197) and 0.92% (28/3,049), respectively. No deaths or subsequent complications were reported during the course of the study. There was no significant difference in the incidence of severe adverse events between the single and co-administration groups for both vaccines: PRP-T, 0.55% (31/5,662) versus 0.81% (45/5,535;  $P = 0.11$ ); PCV7, 0.88% (11/1,247) versus 0.94% (17/1,802;  $P = 0.86$ ). These results suggest that the simultaneous administration of vaccines including PRP-T and/or PCV7 does not increase the incidence of severe adverse events in Japanese children.

## **Monitoring adverse events of the vaccination campaign against influenza A (H1N1) in the Netherlands**

[Van Puijenbroek E.P.](#), [Broos N.](#), [Van Grootheest K.](#)

**Drug Safety** 2010 **33:12** (1097-1108)

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Background: In November 2009, a vaccination campaign against Influenza A (H1N1) was started in the Netherlands. The accelerated registration procedure of the vaccines used in this campaign and the use of these vaccines on a large scale indicated a need for real-time safety monitoring. Objective: To describe the processing, analysing and performing of signal detection by the Netherlands Pharmacovigilance Centre (Lareb) on reports of adverse events following immunization (AEFI) with respect to the two pandemic influenza vaccines, Focetria® and Pandemrix®, used in the Netherlands. The secondary aim is to provide a summary of the results of the safety monitoring of both vaccines. Study Design: Description of the process of collecting information and analysis of the safety monitoring of the pandemic vaccines during the vaccination campaign against H1N1 in the Netherlands. An observational study on adverse events following immunization (AEFIs) associated with vaccines used in this campaign was conducted. Results: The use of a dedicated web form with predefined AEFIs enabled an efficient way of processing and analysing the reports, resulting in a close to real-time monitoring of the safety of the vaccines. From 1 November 2009 until 1 March 2010, 7534 reports concerning one or more AEFIs possibly related to the administration of both vaccines were



received. 2788 of the reports related to Focetria® and 4746 of the reports related to Pandemrix®. The total time between receiving the reports and completion was longer for the serious reports (average 2.8 days) compared with the non-serious reports (average 0.8 days). The profile of the reported adverse events is comparable with the information provided in the Summary of Product Characteristics (SPC). Differences in reported AEFIs between both vaccines may be caused by bias and confounding due to the different populations for which these vaccines have been used. No signals of possible batch-related problems were detected for either vaccine. © 2010 Adis Data Information BV. All rights reserved.

### **Safety of Zostavax™-A cohort study in a managed care organization**

[Baxter R.](#), [Tran T.N.](#), [Hansen J.](#), [Emery M.](#), [Fireman B.](#), [Bartlett J.](#), [Lewis N.](#), [Saddier P.](#)

**Vaccine** 2012 **30:47** (6636-6641)

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Background: Zostavax™ is a live, attenuated varicella-zoster virus vaccine indicated for the prevention of herpes zoster (shingles). An observational post-licensure (Phase IV) study was conducted at Kaiser Permanente Northern California (KPNC), a US managed care organization, to assess the safety of zoster vaccine in people 60 years of age or older, vaccinated in routine medical care. Methods: We performed a cohort study, comparing rates of clinical events resulting in hospitalizations or emergency department visits in a 42-day risk time period immediately following vaccination with rates in the same cohort in a subsequent comparison time period. The study data were reviewed and interpreted by an external safety review committee of 3 independent experts. Results: Approximately 29,000 people ≥ 60 years of age were vaccinated with zoster vaccine from July 2006 to November 2007. Of the 386 comparisons performed for the main analysis, 4 had an increased relative risk with a nominal p-value. ≤ 0.05. After medical records review, the timing of these conditions and procedures was found to be often prior to vaccination, and no clear increase in health events was observed in the risk period following vaccination compared to later. Persons receiving zoster vaccine appeared to be in their optimal health at the time of vaccination, which led to an apparent protective effect of the vaccine for some health outcomes, due to the study design. Conclusions: There was no evidence of a safety concern for zoster vaccine. © 2012 Elsevier Ltd.

### **An early (3-6 weeks) active surveillance study to assess the safety of pandemic influenza vaccine Focetria® in a province of Emilia-Romagna region, Italy - Part One**

[Candela S.](#), [Pergolizzi S.](#), [Ragni P.](#), [Cavuto S.](#), [Nobilio L.](#), [Di Mario S.](#), [Dragosevic V.](#), [Groth N.](#), [Magrini N.](#)

**Vaccine** 2013 **31:10** (1431-1437)

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Introduction: An observational, non-comparative, prospective, surveillance study of individuals vaccinated with the MF59-adjuvanted A/H1N1 influenza vaccine, Focetria®, (Novartis Vaccines & Diagnostics, Siena, Italy), was



performed in Italy during the 2009 A/H1N1 influenza pandemic. Method: This study assessed the short-term (six-week) safety profile of the investigational vaccine in real time. After vaccination (N= 7943), adverse events (AE) were assessed using both active (telephone) and passive (healthcare database) follow-up in enrolled vaccinated subjects, including infants (6-23 months), pregnant women, and the immunosuppressed. The treating physicians of all subjects experiencing AEs post-vaccination were consulted for clinical information on the conditions reported. All AEs were coded according to ICD-10. Results: A total of 1583 AEs occurred during the study, 67 (4.2%) of which were serious adverse events (SAEs). One SAE was considered to be possibly related to vaccination (transitory and ill-defined neurologic disorder experienced by a 16-year-old asthmatic male). Three adverse events of special interest (AESI) were identified (convulsions experienced by two epileptic subjects), none of which were considered to be vaccine-related. Six individuals died during the study period, in each case the cause of death was not related to vaccination (four cases of severe underlying co-morbidity, one case of psychoactive drug misuse, and one case of acute myocardial infarction). Conclusions: No cases of clinically relevant AEs, SAEs, or AESI were observed within a six-week period of vaccine administration. In accordance with existing clinical and post-marketing safety data, the results of this active surveillance study demonstrate a good safety profile for the MF59-adjuvanted A/H1N1 vaccine, Focetria, within the general population. © 2012 Elsevier Ltd.

### **Safety of AS03-adjuvanted split-virion H1N1 (2009) pandemic influenza vaccine: A prospective cohort study**

[Nazareth I.](#), [Tavares F.](#), [Rosillon D.](#), [Haguinet F.](#), [Bauchau V.](#)

**BMJ Open** 2013 **3:2** Article Number 001912

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Objectives: To assess the safety of an AS03- adjuvanted split virion H1N1 (2009) vaccine (Pandemrix) in persons vaccinated during the national pandemic influenza vaccination campaign in the UK. Design: Prospective, cohort, observational, postauthorisation safety study. Setting: 87 general practices forming part of the Medical Research Council General Practice Research Framework and widely distributed throughout England. Participants: A cohort of 9143 individuals aged 7 months to 97 years who received at least one dose of the AS03-adjuvanted H1N1 pandemic vaccine during the national pandemic influenza vaccination campaign in the UK was enrolled. 94% completed the 6-month follow-up. Exclusion criteria were previous vaccination with other H1N1 pandemic vaccine and any child in care. Primary and secondary outcome measures: Medically attended adverse events (MAEs) occurring within 31 days after any dose, serious adverse events (SAEs) and adverse events of special interest (AESIs) following vaccination were collected for all participants. Solicited adverse events (AEs) were assessed in a subset of participants. Results: MAEs were reported in 1219 participants and SAEs in 113 participants during the 31-day postvaccination period. The most frequently reported MAEs and SAEs were consistent with events expected to be reported during the winter season in this population: lower respiratory tract infections, asthma and pneumonia. The most commonly reported solicited AEs were irritability in young children aged <5 years (61.8%), muscle aches in children aged 5-17 years (61.9%) and adults (46.9%). 18 AESIs, experienced by 14 patients, met the



criteria to be considered for the observed-to-expected analyses. AESIs above the expected number were neuritis (1 case within 31 days) and convulsions (8 cases within 181 days). There were 41 deaths during the 181-day period after vaccination, fewer than expected. Conclusions: Results indicate that the AS03-adjuvanted H1N1 pandemic vaccine showed a clinically acceptable reactogenicity and safety profile in all age and risk groups studied.

**A postlicensure evaluation of the safety of Ann Arbor strain live attenuated influenza vaccine in children 24-59 months of age**

[Toback S.L.](#), [Ambrose C.S.](#), [Eaton A.](#), [Hansen J.](#), [Aukes L.](#), [Lewis N.](#), [Wu X.](#), [Baxter R.](#)

**Vaccine** 2013 **31:14** (1812-1818)

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Background: In the **United States**, live attenuated influenza vaccine (LAIV) was initially approved for use in individuals aged 5-49 years in 2003, which was extended to individuals aged 2-49 years in 2007. At that time, a postlicensure commitment was made to describe the safety of LAIV within a cohort of eligible children aged 2-5 years. Methods: A prospective observational postmarketing study was conducted to evaluate the safety of LAIV. Rates of medically attended events (MAEs) and serious adverse events (SAEs) in eligible children aged 24-59 months receiving LAIV as part of routine care from October 2007 to March 2010 were compared with rates in a within-cohort self-control, as well as matched unvaccinated and matched trivalent inactivated influenza vaccine (TIV)-vaccinated controls. Children with asthma and other high-risk medical conditions before vaccination were excluded. All MAEs and SAEs through 42 days postvaccination and all hospitalizations and deaths through 6 months postvaccination were analyzed. Statistical significance was declared without multiplicity adjustment. Results: A total of 28,226 unique LAIV recipients were matched with similar numbers of TIV-vaccinated and unvaccinated children. Of 4696 MAE incidence rate comparisons, 83 (1.8%) were statistically significantly higher and 221 (4.7%) were statistically significantly lower in LAIV recipients versus controls. No pattern of MAE rate differences suggested a safety signal with LAIV. Asthma/wheezing MAEs were not statistically increased in LAIV recipients. No anaphylaxis events occurred within 3 days postvaccination. Rates of SAEs were similar between LAIV and control groups. Conclusions: Results of this postlicensure evaluation of LAIV safety in US children are consistent with preapproval clinical studies and Vaccine Adverse Event Reporting System reports, both of which demonstrated no significant increase in asthma/wheezing events or other adverse outcomes among eligible children aged 24-59 months who received LAIV. © 2013 Elsevier Ltd.

**Post-marketing safety evaluation of a tetanus toxoid, reduced diphtheria toxoid and 3-component acellular pertussis vaccine administered to a cohort of adolescents in a united states health maintenance organization**

[Klein N.P.](#), [Hansen J.](#), [Lewis E.](#), [Lyon L.](#), [Nguyen B.](#), [Black S.](#), [Weston W.M.](#), [Wu S.](#), [Li P.](#), [Howe B.](#), [Friedland L.R.](#)

**Pediatric Infectious Disease Journal** 2010 **29:7** (613-617)



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**Background:** Prelicensure clinical studies may not include sufficient numbers of subjects to assess the potential for rare postvaccination adverse events. The aim of this postlicensure study (NCT00297856) was to evaluate uncommon outcomes following vaccination with a tetanus, reduced-antigen-content diphtheria, and acellular pertussis vaccine (Tdap, Boostrix GlaxoSmithKline) in a large adolescent cohort. **Methods:** We monitored safety outcomes among 13,427 10 to 18-year-old adolescents enrolled in the Northern California Kaiser Permanente Health Care Plan who received Tdap vaccination as part of their normal health care. Subjects were evaluated using self-control analysis comparing days 0 to 29 to days 30 to 59 postvaccination for neurologic events, hematologic events and allergic reactions. We evaluated new onset chronic illnesses within 6 months of Tdap vaccination by comparing with historical Td controls matched for age at vaccination, season, sex, and geographic area. We also compared the incidence of events of interest between the Tdap and historical cohorts as exploratory analyses. **Results:** No increased risk for medically attended neurologic (odds ratio [OR], 0.962; 95% confidence interval [CI], 0.533-1.733) or allergic reactions (OR, 1.091; 95% CI, 0.441-2.729) was observed following Tdap vaccination when comparing the first 30 postvaccination days to the second 30 postvaccination days. There was one hematologic event within 30 days of Tdap, compared with 0 events within days 30 to 59 ( $P = 1.0$ ). When compared with matched historical Td recipients, no increase in new onset chronic illnesses (OR, 0.634; 95% CI, 0.475-0.840) was seen after Tdap. No deaths occurred in the Tdap cohort during the study. **Conclusions:** This study provides no evidence for an increased risk for neurologic, hematologic, allergic events, or new onset of chronic illnesses among adolescents vaccinated with Tdap. © 2010 by Lippincott Williams & Wilkins.

**Adverse events associated with pandemic influenza vaccines:  
Comparison of the results of a follow-up study with those coming from  
spontaneous reporting**

[Carvajal A.](#), [Ortega P.G.](#), [Sáinz M.](#), [Velasco V.](#), [Salado I.](#), [Martín Arias L.H.](#),  
[Eiros J.M.](#), [Pérez Rubio A.](#), [Castrodeza J.](#)

**Vaccine** 2011 **29:3** (519-522)

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Prior to marketing of pandemic influenza vaccines, the only safety data were those from clinical trials. The objective of this study was to compare information coming from spontaneous reporting with that systematically collected in a formal observation study; this also permits to further evaluate safety of pandemic influenza vaccines in the targeted patients' population. Out of a sample of 507 vaccinated subjects, 103 (20.3%) developed some complication. In the same period 83 reports corresponding to all vaccinated people of **Castilla y León** ( $n=131,462$ ) were collected. Severe cases were 1 (1%) and 7 (8.4%), respectively, with the two procedures. The spontaneous reporting rate was 322-fold lower than that identified through the follow-up study; when considered the severe cases, it was 37-fold lower. Under certain circumstances reporting might be performing better than usual due to strengthening of the surveillance system. Adverse events observed for the pandemic H1N1 vaccines lie within the expected safety profile for common



events with influenza vaccines. An overall benefit-risk assessment of these vaccines should be done. © 2010.

### **Observational safety study of febrile convulsion following first dose MMRV vaccination in a managed care setting**

[Jacobsen S.J.](#), [Ackerson B.K.](#), [Sy L.S.](#), [Tran T.N.](#), [Jones T.L.](#), [Yao J.F.](#), [Xie F.](#), [Craig Cheetham T.](#), [Saddier P.](#)

**Vaccine** 2009 **27:34** (4656-4661)

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Background: A combined measles, mumps, rubella, varicella live vaccine (MMRV, Merck and Co., Inc., US) was recently licensed in **the US**. Pre-licensure clinical trial data showed a significant increase in fever in days 5-12 following MMRV vaccination as compared to the vaccines given separately (MMR + V). This post-licensure retrospective cohort study was undertaken to assess the incidence of febrile convulsion following MMRV. Methods: Children ages 12-60 months who received a first dose of MMRV in February 2006-June 2007 in a managed care organization were included in the study. Subjects were optimally matched on age, sex, and calendar date of vaccination to children who received MMR + V concomitantly in November 2003-January 2006, before MMRV licensure. Potential cases of febrile convulsion were identified through administrative data and adjudicated by expert panel, according to pre-specified criteria. Results: During the 30 days post-vaccination, there were 128 and 94 potential convulsion cases among the 31,298 children in the MMRV and MMR + V cohorts, respectively. After review of available medical charts and adjudication, there were 84 cases of confirmed febrile convulsion, 44 (1.41/1000) and 40 (1.28/1000) in the MMRV and MMR + V cohorts, respectively (RR = 1.10, 95% CI = 0.72, 1.69). In days 5-12 following vaccination, a pre-specified period of interest, the respective numbers were 22 (0.70/1000) and 10 (0.32/1000) (RR = 2.20, 95% CI = 1.04, 4.65). Conclusion: These data suggest that the risk of febrile convulsion is increased in days 5-12 following vaccination with MMRV as compared to MMR + V given separately during the same visit, when post-vaccination fever and rash are also increased in clinical trials. While there was no evidence of an increase in the overall month following vaccination, the elevated risk during this time period should be communicated and needs to be balanced with the potential benefit of a combined vaccine. © 2009 Elsevier Ltd. All rights reserved.

### **U.S. Postlicensure safety surveillance for adolescent and adult tetanus, diphtheria and acellular pertussis vaccines: 2005-2007**

[Chang S.](#), [O'Connor P.M.](#), [Slade B.A.](#), [Woo E.J.](#)

**Vaccine** 2013 **31:10** (1447-1452)

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Background: Pre-licensure clinical trials for two U.S. licensed tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccines did not reveal any major safety concerns. However, routine use in large adolescent and adult populations could reveal rare and potentially serious adverse events (AEs). Methods: To characterize reported AEs following Tdap vaccination and identify potential safety concerns warranting further evaluation, we analyzed data from



the Vaccine Adverse Event Reporting System (VAERS) and assessed the frequency and proportions of AEs and reporting rates (reports per 100,000 vaccine doses distributed). Results: A total of 2090 reports (7% were serious; 55% listed Tdap alone) involving Tdap vaccines were submitted to VAERS May 2005-June 2007. The crude reporting rate was 10.2 per 100,000 vaccine doses distributed. The median age of vaccinees was 22 years, and the female to male ratio was about 2 to 1. The majority of reports described common local and systemic signs and symptoms, such as injection site reactions, fever, and headache. Rarely reported AEs included myopericarditis, demyelinating diseases of the central nervous system, Guillain-Barré Syndrome, syncope, encephalopathy/encephalitis, seizure, Bell's palsy, anaphylaxis, and thrombocytopenia. Conclusions: Because adolescents and adults were not routinely vaccinated against pertussis in the past, this surveillance summary provides important - and reassuring - information about the use of Tdap in these age groups. Although subject to the limitations of passive surveillance, the findings of this VAERS review support the pre-licensure clinical trial data with regard to the safety of the U.S. licensed Tdap vaccines. Continued monitoring of clinically significant AEs that are temporally associated with Tdap vaccination and further assessment of such events using controlled observational studies may provide additional information about the safety of these vaccines. © 2012.

**Immunogenicity and safety of the bivalent HPV vaccine in female patients with juvenile idiopathic arthritis: A prospective controlled observational cohort study**

[Heijstek M.W.](#), [Scherpenisse M.](#), [Groot N.](#), [Tacke C.](#), [Schepp R.M.](#), [Buisman A.-M.](#), [Berbers G.A.M.](#), [Van Der Klis F.R.M.](#), [Wulffraat N.M.](#)

**Annals of the Rheumatic Diseases** 2014 **73:8** (1500-1507)

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Objectives: To compare the immunogenicity and safety of the bivalent human papillomavirus (HPV)16/18 vaccine between female patients with juvenile idiopathic arthritis (JIA) and healthy female adolescents. Methods: 68 patients and 55 healthy girls aged 12-18 years were included in a prospective controlled observational cohort and were vaccinated at 0, 1 and 6 months. Primary outcomes were immunogenicity expressed as seropositivity rate after three vaccine doses at 7 and 12 months and HPV-specific geometric mean antibody concentrations. Secondary outcomes were HPV16/18-specific memory B cell responses in a subset of participants and safety, defined as adverse events and the effect of vaccination on JIA disease activity. Results: All participants were seropositive for HPV16 and HPV18 at 7 months. One patient turned seronegative at 12 months for HPV16/18. No significant differences were found between patients and controls in HPV-specific antibody concentrations; however, antibody concentrations were consistently lower in patients. No effect of methotrexate on HPV16 antibodies ( $p=0.79$ ) or HPV18 antibodies ( $p=0.37$ ) was detected. All patients on anti-TNF $\alpha$  treatment were seropositive after vaccination. The kinetics of HPV16/18 memory B cell responses was comparable between patients and controls, but the magnitude of B cell responses at 7 and 12 months appeared lower in patients. No relevant differences in adverse events were found. HPV vaccination did not aggravate JIA disease. Conclusions: The bivalent HPV16/18 vaccine is immunogenic and well tolerated in JIA



patients. However, HPV-specific antibodies and B cell responses tended to be lower in patients compared with healthy controls.

## General articles

### **Use of the self-controlled case-series method in vaccine safety studies: Review and recommendations for best practice**

[Weldeselassie Y.G.](#), [Whitaker H.J.](#), [Farrington C.P.](#)

**Epidemiology and Infection** 2011 **139:12** (1805-1817)

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The self-controlled case-series method was originally developed to investigate potential associations between vaccines and adverse events, and is now commonly used for this purpose. This study reviews applications of the method to vaccine safety investigations in the period 1995-2010. In total, 40 studies were reviewed. The application of the self-controlled case-series method in these studies is critically examined, with particular reference to the definition of observation and risk periods, control of confounders, assumptions and potential biases, methodological and presentation issues, power and sample size, and software. Comparisons with other study designs undertaken in the papers reviewed are also highlighted. Some recommendations are presented, with the emphasis on promoting good practice. © 2011 Cambridge University Press.

### **Registration of observational studies: Is it time?**

[Williams R.J.](#), [Tse T.](#), [Harlan W.R.](#), [Zarin D.A.](#)

**CMAJ** 2010 **182:15** (1638-1642)

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Observational studies form an important part of the medical evidence base, particularly for assessing rare adverse events and long-term effectiveness of medications and devices. 1 However, observational studies, like interventional studies (clinical trials), are subject to publication bias and reporting bias. 2–4 Registration of clinical trials is a widely recognized tool for facilitating complete public reporting. 5 Registration of observational studies has received less attention, although interest is growing. 6–8 Because existing registries (e.g., ClinicalTrials.gov) accommodate observational studies, and the rationale and benefits of registration are similar, we ask the scientific community and other stakeholders to consider the systematic, prospective registration of observational studies.

### **A scan statistic for identifying optimal risk windows in vaccine safety studies using self-controlled case series design**

[Xu S.](#), [Hambidge S.J.](#), [Mcclure D.L.](#), [Daley M.F.](#), [Glanz J.M.](#)

**Statistics in Medicine** 2013 **32:19** (3290-3299)

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In the examination of the association between vaccines and rare adverse events after vaccination in postlicensure observational studies, it is challenging to define appropriate risk windows because prelicensure RCTs provide little insight on the timing of specific adverse events. Past vaccine safety studies have often used prespecified risk windows based on prior publications, biological understanding of the vaccine, and expert opinion. Recently, a data-driven approach was developed to identify appropriate risk windows for vaccine safety studies that use the self-controlled case series design. This approach employs both the maximum incidence rate ratio and the linear relation between the estimated incidence rate ratio and the inverse of average person time at risk, given a specified risk window. In this paper, we present a scan statistic that can identify appropriate risk windows in vaccine safety studies using the self-controlled case series design while taking into account the dependence of time intervals within an individual and while adjusting for time-varying covariates such as age and seasonality. This approach uses the maximum likelihood ratio test based on fixed-effects models, which has been used for analyzing data from self-controlled case series design in addition to conditional Poisson models. © 2013 John Wiley & Sons, Ltd.

### **Monitoring and assessing vaccine safety: A European perspective**

[Lopalco P.L.](#), [Johansen K.](#), [Ciancio B.](#), [De Carvalho Gomes H.](#), [Kramarz P.](#), [Giesecke J.](#)

**Expert Review of Vaccines** 2010 **9:4** (371-380)

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The success of vaccination programs is an uncontroversial reality - in Europe as well as worldwide. On the other hand, the perceived risk of adverse events in the general public is the most important threat for implementing successful vaccination programs in Europe. For this reason, monitoring and assessing vaccine safety is a priority for public health. Vaccine safety is assessed both before and after vaccine authorization. In postmarketing settings, different activities related to vaccine safety usually involve several different stakeholders. In 2005, a new EU agency, the European Centre for Disease Prevention and Control, was established with the aim to strengthen Europe's defences against infectious diseases. Implementing stable links between different stakeholders and defining clear roles in the EU is paramount in order to provide optimal and transparent information on adverse reactions following immunization, with the final goal of increasing compliance to safe and effective vaccination programs. © 2010 Expert Reviews Ltd.

### **A study of adverse drug reactions in patients admitted to intensive care unit of a tertiary care teaching rural hospital**

[Kathiria J.M.](#), [Sattigeri B.M.](#), [Desai P.M.](#), [Patel S.P.](#)

**International Journal of Pharmacy and Pharmaceutical Sciences** 2013 **5:1** (160-163)

Adverse drug reactions (ADRs) are the common problems faced in the setups like ICU where the poly pharmacy is involved in treating the patients. Control of such events is possible if the culpable drug is known or if it is identified and



reported. However, reporting of adverse drug reactions still remains in its infancy for problems in many. Awareness about adverse drug reactions can decrease irrational use of medicines, poly pharmacy and adverse drug-drug interactions. A prospective, observational and non-interventional study was conducted over a period of 18 months in medical ICU of Dhiraj hospital, Piparia with the goal to highlight the responsibility of health care professionals in preventing, identifying, diagnosis, treating and reporting ADRs. The patients were monitored daily for ADRs. The data was analyzed for demographic parameters. The causality relationship between suspected drugs and the reactions were assessed by using various standard causality assessment scales. 1000 patients were enrolled for the study. Out of these 45 patients developed ADRs. Of these 27 males and 18 females developed ADRs showing male predominance (2. 7%). The ADRs increased with increasing number of drugs administered. The drug class most commonly implicated with ADRs was antibiotics 24(53. 33%). The system most commonly involved with an ADR was gastrointestinal tract 26. 67%. Most commonly reported reaction were hypoglycemia (13. 33%) and Rash (11. 11%).

## Pregnancy

### **H1N1 influenza vaccination during pregnancy**

[Fell D.B.](#), [Dodds L.](#), [McNeil S.](#), [MacDonald N.E.](#)

**BMJ (Online)** 2014 **348** Article Number g3500

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H1N1 safety data look reassuring, but we need ongoing surveillance of all influenza vaccines given to pregnant women

Risks to pregnant women from influenza infection have long been recognized.<sup>1</sup> The recent 2009-10 H1N1 pandemic was no exception—pregnant women were at higher risk of severe H1N1 influenza illness compared with the general population,<sup>2</sup> and those with H1N1 influenza had higher rates of adverse pregnancy outcomes than did uninfected pregnant women.<sup>3</sup> Despite limited safety data for use of the monovalent H1N1 vaccines in pregnancy, pregnant women were widely prioritized for H1N1 vaccination programs.<sup>4</sup> Fortunately, enhanced surveillance of pregnant women during the pandemic has enabled retrospective evaluation of the safety of monovalent H1N1 vaccine in obstetric populations around the world.

### **Influenza H1N1 vaccination and adverse pregnancy outcome**

[Ludvigsson J.F.](#), [Zugna D.](#), [Cnattingius S.](#), [Richiardi L.](#), [Ekblom A.](#), [Örtqvist Å.](#), [Persson I.](#), [Stephansson O.](#)

**European Journal of Epidemiology** 2013 **28:7** (579-588)

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Although vaccines against influenza can reduce maternal morbidity and mortality, large-scale data on adverse effects in the offspring are scarce.



Historical cohort study in Stockholm County, Sweden. We linked H1N1 vaccination data (Pandemrix®, a mono-valent AS03 adjuvanted H1N1 vaccine) with pregnancy and birth data from 21,087 women with singleton offspring conceived between February 2009 and January 2010 (vaccinated during pregnancy: n = 13,297 vs. unvaccinated: n = 7,790). Data were analysed by conceptualizing the observational cohort as a series of nested cohorts defined at each week of gestation. Logistic regression estimated odds ratios (ORs) for low birth weight (LBW, <2,500 g), preterm birth (<37 completed weeks), small-for-gestational age (SGA, <10th percentile of the gestational age-specific birth weight within the cohort), low 5-min Apgar score (<7), and caesarean section. Data were adjusted for potential confounders, including maternal age, body mass index, smoking, parity, civil status and comorbidities. Compared with infants of non-vaccinated women, infants of vaccinated women had similar adjusted ORs (95 % CI) for LBW (0.91; 0.79-1.04), preterm birth (0.99; 0.89-1.10), SGA (0.97; 0.90-1.05), low Apgar score (1.05, 0.84-1.31), and a marginal risk reduction for caesarean section (0.94, 0.89-0.99). H1N1 vaccination during pregnancy, using an AS03-adjuvanted vaccine, does not appear to adversely influence offspring risks of LBW, preterm birth, SGA, or low Apgar score. Our results suggest that this vaccine is safe for the offspring when used in different stages of pregnancy. © 2013 Springer Science+Business Media Dordrecht.

**Influenza H1N1 (swine flu) vaccination: A safety surveillance feasibility study using self-reporting of serious adverse events and pregnancy outcomes**

[Mackenzie I.S.](#), [Macdonald T.M.](#), [Shakir S.](#), [Dryburgh M.](#), [Mantay B.J.](#), [Mcdonnell P.](#), [Layton D.](#)

**British Journal of Clinical Pharmacology** 2012 **73:5** (801-811)

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**Aims:** During the global H1N1 influenza A (swine flu) pandemic 2009-2010, swine flu vaccines were expeditiously licensed and a mass vaccination programme for high risk groups, including pregnant women, was introduced in the UK. This pilot active safety surveillance study was performed to establish the feasibility of rapidly monitoring the new swine flu vaccines in large patient numbers receiving or offered the vaccination under normal conditions of use within a short time frame. **Methods:** A cohort design with safety data capture through modern technologies was carried out in Scotland, UK during the winter swine flu vaccination programme 2009-2010 in individuals receiving or offered the swine flu vaccination. The main outcome measures were self-reported serious adverse events (SAEs) and pregnancy outcomes. **Results:** The cohort comprised 4066 people; 3754 vaccinated and 312 offered the vaccination but not vaccinated. There were 939 self-reported events (838 different events), 53 judged to fit SAE criteria by the investigators, with nine judged as possibly, probably or definitely vaccine related. None of the seven deaths (six in vaccinees) were judged as vaccine related. One hundred and twenty-eight women reported 130 pregnancies during the study with 117 pregnant at study start. There were reports of four miscarriages in three women and six possible congenital abnormalities in live births. **Conclusions:** Overall, no significant safety issues were identified. The methodology and use of modern technologies to collect safety data from large numbers of patients was successful and could



be used again in similar safety studies. © 2011 The Authors. British Journal of Clinical Pharmacology © 2011 The British Pharmacological Society.

### **A(H1N1)v2009: A controlled observational prospective cohort study on vaccine safety in pregnancy**

[Oppermann M.](#), [Fritzsche J.](#), [Weber-Schoendorfer C.](#), [Keller-Stanislawski B.](#), [Allignol A.](#), [Meister R.](#), [Schaefer C.](#)

**Vaccine** 2012 **30:30** (4445-4452)

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Background: A(H1N1)v2009 influenza vaccination of pregnant women was a challenge for health care providers, as little safety data were available. Methods: We prospectively followed the pregnancies of women who were vaccinated at any time during pregnancy or  $\leq 4$  weeks prior to conception and compared these outcomes to a control cohort matched by the estimated date of birth. Primary endpoints: rate of spontaneous abortion and major malformations. Secondary endpoints: preeclampsia, gestational age at birth, and birth weight. Results: Pregnancy outcome of 323 women immunized with adjuvanted or non-adjuvanted A(H1N1)v2009 influenza vaccines from 2009-09-28 to 2010-03-31 were compared to 1329 control subjects. The risk for spontaneous abortions (HR 0.89; 95% CI 0.36-2.19) and the rate of major malformations (all trimesters: OR 0.87; 95% CI 0.38-1.77; preconception and first trimester exposure: OR 0.79; 95% CI 0.13-2.64) did not vary between the two cohorts. Furthermore, there was no increase in preeclampsia, prematurity, and intrauterine growth retardation in the vaccinated cohort. Conclusion: The results of our study do not indicate a risk for the pregnant woman and the developing embryo/fetus after H1N1 vaccination. We provide and apply methods novel in observational studies on pregnancy outcome, especially if a single dose exposure is investigated. © 2012 Elsevier Ltd.

### **Maternal safety of trivalent inactivated influenza vaccine in pregnant women**

[Nordin J.D.](#), [Kharbanda E.O.](#), [Benitez G.V.](#), [Nichol K.](#), [Lipkind H.](#), [Naleway A.](#), [Lee G.M.](#), [Hambidge S.](#), [Shi W.](#), [Olsen A.](#)

**Obstetrics and Gynecology** 2013 **121:3** (519-525)

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OBJECTIVE: To estimate the risks for medically attended events occurring within 42 days of receiving trivalent inactivated influenza vaccine and to evaluate specific risks of first-trimester vaccination. METHODS: This retrospective observational cohort study compared rates of medically attended adverse events in trivalent inactivated influenza-vaccinated and unvaccinated pregnant women in the Vaccine Safety Datalink. Using a Poisson distribution and log link, we calculated maternal adjusted incident rate ratios for composite safety outcomes for the full cohort and the subset vaccinated during the first trimester. RESULTS: The cohort included 75,906 vaccinated (28.4% in the first trimester) and 147,992 unvaccinated women matched by age, site, and pregnancy start date. In the first 3 days after vaccination, trivalent inactivated influenza vaccine was not associated with increased risk of specified medically attended events, including allergic reactions, cellulitis, and seizures (full cohort



adjusted incident rate ratio 1.12, 95% confidence interval [CI] 0.81-1.55; P=.48; first-trimester adjusted incident rate ratio .97, 95% CI 0.53-1.78; P=.93). In the first 42 days, no incident cases of Guillain-Barré syndrome, optic neuritis, transverse myelitis, or Bells palsy were identified. Trivalent inactivated influenza vaccine was not associated with thrombocytopenia (full cohort adjusted incident rate ratio 0.90, 95% CI 0.68-1.19; P=.45; first-trimester adjusted incident rate ratio 0.56, 95% CI 0.22-1.39; P=.21) or an acute neurologic event (full cohort adjusted incident rate ratio 0.92, 95% CI 0.54-1.6; P=.75; first-trimester adjusted incident rate ratio 1.05, 95% CI 0.46-2.38; P=.91). **CONCLUSIONS:** Receipt of trivalent inactivated influenza vaccine during pregnancy was not associated with increased risk of adverse events in the 42 days after vaccination, supporting its safety for the mother. © 2013 by The American College of Obstetricians and Gynecologists.

### **Safety of seasonal influenza and influenza A (H1N1) 2009 monovalent vaccines in pregnancy**

[Moro P.L.](#), [Tepper N.K.](#), [Grohskopf L.A.](#), [Vellozzi C.](#), [Broder K.](#)

**Expert Review of Vaccines** 2012 **11:8** (911-921)

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Inactivated influenza vaccines have been given to pregnant women since 1964. Since 2004, the Advisory Committee on Immunization Practices has recommended that pregnant women receive trivalent inactivated influenza vaccine at any time during pregnancy. Studies conducted before 2009 did not identify any safety concerns after trivalent inactivated influenza vaccine in mothers or their infants. During the 2009-2010 influenza A (H1N1) influenza vaccination program, several monitoring systems were established or enhanced to assess whether adverse events were associated with H1N1 2009 monovalent vaccines (2009 H1N1 influenza vaccines). Data from these systems did not identify any safety concerns in pregnant women who received 2009 H1N1 influenza vaccines or their infants. Although live attenuated influenza vaccines are not recommended in pregnant women, a small number of studies have not shown any safety concern among pregnant women or their infants who were inadvertently exposed to these vaccines. This review summarizes US and international safety data for influenza vaccines in pregnant women with an emphasis on 2009 H1N1 influenza vaccines. © 2012 2012 Expert Reviews Ltd.

### **Safety of MF59-adjuvanted A/H1N1 influenza vaccine in pregnancy: A comparative cohort study**

[Heikkinen T.](#), [Young J.](#), [Van Beek E.](#), [Franke H.](#), [Verstraeten T.](#), [Weil J.G.](#), [Della Cioppa G.](#)

**American Journal of Obstetrics and Gynecology** 2012 **207:3** (177.e1-177.e8)

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Objective: The 2009-2010 A/H1N1 pandemic provided a unique setting to study the safety of MF59-adjuvanted vaccination in pregnancy. Study Design: This was an observational cohort study of the safety of an MF59-adjuvanted A/H1N1 vaccine (Focetria) conducted among 4508 pregnant women (2295 vaccinated vs 2213 unvaccinated), with 3 month follow-up of neonates. Results: No maternal



deaths or abortions occurred among the vaccinated women. No differences between the vaccinated and unvaccinated cohorts were observed for gestational diabetes, preeclampsia, stillbirth, low birthweight, neonatal deaths, or congenital malformations. The risk of premature birth was significantly decreased among the vaccinated women (adjusted proportional hazard, 0.69; 95% confidence interval, 0.51-0.92). No differences were observed in rates of congenital malformations after vaccination in the first (2.1%), second (2.7%), or third (2.1%) trimesters. Conclusion: There was no evidence of a safety risk for MF59-adjuvanted A/H1N1 vaccination in pregnant women; protection was observed against premature birth. © 2012 Mosby, Inc.

**Pharmacovigilance monitoring of a cohort of pregnant women vaccinated against influenza A(H1N1) variant virus in the Nord-Pas de Calais region of northern France**

[Auffret M.](#), [Béné J.](#), [Gautier S.](#), [Moreau-Crépeaux S.](#), [Caron J.](#)

**European Journal of Obstetrics Gynecology and Reproductive Biology** 2013 **170:1** (114-118)

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**Objective** During the 2009-2010 influenza A variant virus (A(H1N1)v) pandemic in France, a national pharmacovigilance program was set up to monitor vaccinated, pregnant women, especially the reactogenicity of the vaccine and its impact on the outcome of pregnancy and on the newborn. Here, we present the results for the cohort of pregnant women constituted in the Nord-Pas de Calais region of northern France. **Study design** Vaccinated pregnant women were included in the study by the region's vaccination centers between November 2009 and April 2010. **Results** Eight hundred and six pregnant women were included and 781 were followed up until delivery. The risk of adverse events after vaccination and the maternal, fetal and neonatal medical conditions in our cohort did not appear different from the risk observed in the general population. **Conclusions** Our results suggest that A(H1N1)v vaccination of pregnant women did not have an adverse

## **Epidemiology study**

**Prevalence of cervical human papillomavirus infection and types among women immigrated to Sicily, Italy**

[Giovannelli L.](#), [Vassallo R.](#), [Matranga D.](#), [Affronti M.](#), [Caleca M.P.](#), [Bellavia C.](#), [Perino A.](#), [Ammatuna P.](#)

**Acta Obstetricia et Gynecologica Scandinavica** 2009 **88:6** (737-742)

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We determined the prevalence of human papillomavirus (HPV) cervical infection and HPV genotypes among 115 women immigrating to Sicily (Italy), with regard to abnormal cytology and socio-behavioral characteristics in a cross-sectional, observational study. Information was collected with the help of cultural mediators/translators. HPV-DNA was assayed by the INNOLiPA HPV



assay and a nested PCR/sequencing method. Sixty (52.2%) women came from sub-Saharan Africa and 55 (47.8%) from Eastern Europe. HPV infection was found in 55 (47.8%) women. The most frequent types were the oncogenic types HPV-16 (7.8%), HPV-18 and 51 (6.0% each), HPV-52 (5.2%), 31, 53, and 68 (4.3% each). Twenty-seven (23.5%) women had cytological abnormalities associated with HPV infection ( $p=0.04$ ). Being single (OR = 2.98; 95%CI: 1.30-6.84) and parity (OR = 0.29; 95%CI: 0.12-0.65) were consistent predictors of HPV infection. Only 21 (18.2%) women returned to collect the results of their Pap and HPV tests. The high prevalence of HPV infection and oncogenic types among immigrant women make them a priority group for cervical cancer screening. Linguistically and culturally appropriate prevention efforts are needed to sensitize immigrant women regarding HPV-related issues and to conduct vaccine strategies for cervical cancer prevention.

### **Epidemiology of rotavirus gastroenteritis among children under 5 years of age in Tunisia - Results of sentinel hospital surveillance 2009 to 2011**

[Soltani M.](#), [Bouanene I.](#), [Trabelsi A.](#), [Harbi A.](#), [Hachicha M.](#), [Amri F.](#), [Boussnina S.](#), [Gueddiche M.N.](#), [Sfar M.T.](#), [Teleb N.](#), [Ben Ghorbel M.](#), [Ben Hamida E.](#)

**Revue d'Epidemiologie et de Sante Publique** 2012 **60:6** (473-480)

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Background: Rotavirus is the major cause of severe acute gastroenteritis among young children. The objectives of this study were to assess the epidemiology, clinical and virological features of community-acquired rotavirus acute gastroenteritis, in children under 5 years of age, hospitalized in Tunisia. Methods: A multicenter prospective observational study was conducted from April 2009 to March 2011, in 11 sentinel pediatric departments. Clinical data and stool samples were collected for all children under 5 years, admitted for acute gastroenteritis. Rotavirus was detected by Elisa immunoassay test and genotyped for G and P by semi-nested multiplex RT-PCR. Result: A total of 621 children were enrolled in this study. Rotavirus was detected in 30.3% of cases (95% CI [26.7-33.9]). The estimated incidence rate of rotavirus acute gastroenteritis was 11 cases/100,000 child-years (95% CI [9.43-12.57]). This infection affected predominantly children aged under 24 months, and occurred mainly in winter (55.3%). Vomiting, fever and dehydration were observed in 79.6%, 69.5% and 57% respectively. Genotype analysis identified four G types (G1, G2, G3 and G4) and 4 P types (P[4], P[6], P[8] and P[9]). The most common G/P combination was G3P[8] (24.4%), followed by G4P[8] (13.3%) and G1P[8] (6.5%). Conclusion: These results highlight the frequency and potential severity of rotavirus acute gastroenteritis in pediatric hospital settings. The present study could provide a sufficient database to make a decision related to the introduction of rotavirus vaccine in Tunisian national immunization program. © 2012 Elsevier Masson SAS.

### **Epidemiology of HPV in HIV-positive and HIV-negative fertile women in cameroon, West Africa**

[Desruisseau A.J.](#), [Schmidt-Grimminger D.](#), [Welty E.](#)

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**Background.** HPV types vary by country and HIV status. There are no data on the prevalent HPV genotypes from Cameroon. **Methods.** We conducted a cross-sectional, observational study on 65 Cameroonian women. Samples were sent for HPV genotyping and Thin Prep analyses. **Results.** 41 out of 61 samples tested (67.2) had HPV subtypes detected. The most common high risk types encountered were: 45 (24.6) and 58 (21.5). HIV-positive women were more likely to test positive for any HPV ( $P=.014$ ), have more than one HPV subtype ( $P=.003$ ), and to test positive for the high risk subtypes ( $P=.007$ ). Of those with high risk HPV, HIV-positive women were more likely to have Thin Prep abnormalities than HIV-negative women ( $P=.013$ ). **Conclusions.** Oncogenic HPV subtypes 45 and 58 were more prevalent than those subtypes carried in the quadrivalent vaccine. Further studies are needed to assess whether the current vaccine will be effective in this region. © 2009 Andrew J. Desruisseau et al.





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## Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)

# Active surveillance of adverse events following childhood immunization in Singapore



Koh Cheng Thoon<sup>a,b,c,\*</sup>, Sally Bee Leng Soh<sup>d</sup>, Woei Kang Liew<sup>a</sup>, Arunan Gunachandran<sup>a</sup>, Natalie Woon Hui Tan<sup>a,b,c</sup>, Chia Yin Chong<sup>a,b,c</sup>, Chee Fu Yung<sup>e</sup>

<sup>a</sup> Department of Paediatric Medicine, KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore 229899, Singapore

<sup>b</sup> Duke-National University of Singapore Graduate Medical School, 8 College Road, Singapore 169857, Singapore

<sup>c</sup> Yong Loo Lin School of Medicine, National University of Singapore, 1E Kent Ridge Road, National University Health System Building (NUH), Singapore 119228, Singapore

<sup>d</sup> Vigilance Branch, Health Products Regulation Group, Health Sciences Authority, 11 Biopolis Way #11-01 Helios Singapore 138667, Singapore

<sup>e</sup> Department of Clinical Epidemiology, Communicable Disease Centre, Institute of Infectious Disease and Epidemiology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433, Singapore

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## ABSTRACT

**Introduction:** In Singapore, reporting of adverse events following immunization (AEFI) was historically passive. In 2009, Health Sciences Authority collaborated with KK Women's and Children's Hospital to perform active surveillance for AEFI. We report the methodology and initial findings of this surveillance following childhood vaccines.

**Methods:** From April 2010 to March 2012, we screened all paediatric admissions for possible relationships to vaccination, excluding elective admissions, and performed causality assessment for each case using standardized definitions for certain, probable, possible and unlikely. Baseline demographics, data on implicated vaccines and clinical details including severity and outcomes were collected. Total hospital admissions were used to calculate rates of AEFI.

**Results:** We screened 45,571 (80%) of 56,526 admissions, and evaluated 1988 (4.4%) children. Median age at presentation was 3.1 months, while median interval from vaccination to symptom onset was 6 days. There were 311 (15.6%) children with AEFI that were considered possibly, probably or certainly associated with vaccines. However, 98.8% recovered without any long-term sequelae. The hospital-based active surveillance of AEFI enabled the detection of a 5-fold increase (95% CI 1.2–33.1) in BCG-associated regional lymphadenitis in April 2010, which triggered follow-up safety analysis to guide public health advice.

**Conclusions:** Hospital-based active surveillance can enhance signal detection and follow-up investigations of AEFI. Subsequently, public health bodies are better equipped to maintain public confidence in vaccination programmes and physicians are able to provide relevant advice to parents. It also allows for a better understanding of risk-benefit ratios of specific vaccines and aids the generation of public health vaccination policy.

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**Abbreviations:** AEFI, adverse event following immunization; BCG, bacillus Calmette–Guérin; DTP, diphtheria–tetanus–pertussis; MMR, measles–mumps–rubella; PCV, pneumococcal conjugate vaccines.

\* Corresponding author at: KK Women's and Children's Hospital, Infectious Disease Service, Department of Paediatric Medicine, Level 3 Offices, 100, Bukit Timah Road, Singapore 229899, Singapore. Tel.: +65 6394 8408; fax: +65 6394 1973.

E-mail addresses: [Thoon.Koh.Cheng@kkh.com.sg](mailto:Thoon.Koh.Cheng@kkh.com.sg) (K.C. Thoon), [Sally.SOH@hsa.gov.sg](mailto:Sally.SOH@hsa.gov.sg) (S.B.L. Soh), [woei\\_kang@yahoo.com.sg](mailto:woei_kang@yahoo.com.sg) (W.K. Liew), [arunan.gunachandran@gmail.com](mailto:arunan.gunachandran@gmail.com) (A. Gunachandran), [Natalie.Tan.WH@kkh.com.sg](mailto:Natalie.Tan.WH@kkh.com.sg) (N.W.H. Tan), [Chong.Chia.Yin@kkh.com.sg](mailto:Chong.Chia.Yin@kkh.com.sg) (C.Y. Chong), [cheefu.yung@gmail.com](mailto:cheefu.yung@gmail.com) (C.F. Yung).

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## 1. Introduction

Immunization has been described to be one of the most cost-effective of all healthcare interventions in history, and, with the possible exception of clean drinking water and modern sanitation, has been estimated to have saved more lives and life-years than all other medical intervention combined [1]. However, because vaccines would usually be given to healthy individuals (as opposed to therapeutic drugs used for the alleviation or cure of disease), there would be an expectation that immunizations were safe and would not lead to harm. As vaccination programmes improve and achieve high coverage, disease burden is expected to fall rapidly. In such scenarios, adverse events following immunization (AEFIs) would



be increasingly scrutinized even if they are rare, and requires monitoring since the benefits of vaccination are quickly forgotten in an environment where exposure to disease is minimal. Any vaccine safety issue, whether real or perceived, could lead to false rumours if not rapidly and effectively managed, with severe consequences on public confidence, immunization coverage and disease incidence [2]. The recent resurgence of measles in the UK and Western Europe, resulting from the now discredited link between MMR and autism, demonstrates the severe public health consequences of such a false association, and could threaten Europe's commitment to eliminate measles in the region by 2015 [3].

AEFI surveillance is wrought with clinical, epidemiologic and statistical challenges, primarily due to the rarity of most adverse events. It would be unlikely that these rare events could be detected during pre-licensure trials, and therefore there would be a need to establish systems to detect AEFI post-licensure. Singapore, similar to most countries in the South-East Asian region, historically employed a passive surveillance system for reporting of adverse events for drugs (including vaccines), which is managed by the Health Science Authority (HSA, the country's national regulatory authority on medical products) [4]. However, a key limitation of such passive surveillance systems was its dependence on clinical vigilance, which varies between clinicians as well as within clinicians at different time points. As a result, the frequency of reported events could be low and vulnerable to chance fluctuations. Furthermore, such systems would be less sensitive in identifying signals from novel adverse events which have not been documented previously. Finally, it would be difficult to verify signals generated from passive surveillance systems to confirm or deny a correlation since the frequency of reports were usually low and had limited statistical power.

In 2009, the Vigilance Branch of HSA (which oversaw passive AEFI surveillance) partnered with KK Women's and Children's Hospital (KKH) to conduct active surveillance for AEFI after influenza vaccination, as part of vaccine safety monitoring following pandemic influenza A (H1N1) public vaccination campaign. [5] When the pandemic subsided, the programme was extended in March 2010 to include active surveillance for all vaccines given in childhood. Prior to the active surveillance programme, between 2005 and 2008 KKH submitted ~7 AEFI reports in children per year to HSA as part of passive surveillance. In this paper, we aim to describe the methodology of a hospital-based, active AEFI surveillance system monitoring childhood vaccines in Singapore, and report its early findings.

## 2. Methods

### 2.1. Data collection

The hospital-based, active surveillance programme was loosely adapted from the Canadian Immunization Monitoring Programme, Active (IMPACT) [6]. The programme consists of 1 full-time equivalent (FTE) of a surveillance coordinator, ~0.1 FTE for participating paediatric infectious diseases and immunology clinicians and clinical epidemiologist, as well as regulatory specialists from HSA (these were separately funded). The hospital (the largest women's and children's hospital in Singapore with ~800 beds, of which 500 were neonatal/paediatric beds) is primarily a tertiary hospital but also functions as a secondary hospital, and admits ~51% of all paediatric inpatients <15 years in Singapore (based on data from Ministry of Health, Singapore; this is out of a population of ~6,15,200 children <15 years in Singapore in 2013). There were >1,70,000 Children's Emergency attendances per year, with a range of paediatric medical and surgical subspecialty services available caring for a variety of complex care patients [7]. An additional ~10% of paediatric

admissions <15 years are seen at the National University Hospital (the only other public sector hospital with paediatric admissions), while the remainder utilize several smaller private hospitals. Healthcare is primarily fee-for-service, with significant subsidies in public sector hospitals [8].

All children who were admitted to KKH between 1st April 2010 and 31st March 2012 were eligible for inclusion in this report. Using electronic healthcare records (and further supported by inpatient clinical notes on paper), all patients admitted with a possible AEFI were identified on a daily basis by manually reviewing their admitting diagnoses and age, followed by recent receipt of immunization; elective admissions (e.g. for surgery, chemotherapy, immunotherapy, diagnostic procedures etc.) were excluded from further screening. Appendix 1 lists relevant criteria used for this initial screen, and the age groups of children eligible for screening essentially reflects the national childhood immunization schedule in Singapore (see Appendix 2). We developed this list based on prior clinical experience, on historical records of reported AEFIs from HSA, and from a review of AEFI literature. Where there was uncertainty regarding whether an admission was an AEFI or not (especially when there was a temporal association with a vaccine), the programme erred on the side of caution by capturing the case and performing further screening.

Apart from demographic information, we collected detailed information on the date and age of vaccination and of symptom onset, date of admission and discharge, and consumption of concurrent medications, from both electronic and paper records (with the exception of the hospital's inpatient clinical notes, all other records (including Emergency department notes, radiology, pharmacy, laboratory data, and discharge summaries) are available electronically). We also collected clinical, laboratory, microbiologic and radiologic details for the admission and presence of any other co-morbidities and concurrent illnesses (especially where there was laboratory confirmation of pathogens that could have led to the admission). Complete vaccination history including vaccination dates, brand, batch numbers, dose, route, site (on the body), and place of vaccination (elicited from patients' Health Booklets [9] or via National Immunization Registry [10]) were also collected. Total numbers of paediatric hospital admissions by month were also extracted for this period.

### 2.2. Causality and assessment

A standardized clinical and causality assessment framework was developed to classify cases identified, by the type of AEFI and into five categories of causality: Certain, Probable, Possible, Unlikely, Unrelated (see Appendices 3 and 4). For the active surveillance, all potential AEFIs captured after the initial screen would first be reviewed by the primary investigator or participating paediatrician; where necessary, urgent cases could be discussed with the rest of the collaborators by phone or email, and appropriate referrals made to the relevant subspecialty (e.g. neurology or allergy). Subsequently, a multidisciplinary panel composed of paediatricians, regulatory specialists from the Vigilance Branch, HSA and clinical epidemiologist would discuss and review the cases on a monthly basis to ensure agreement with the categories assigned; where there was disagreement, cases were assigned according to majority opinion, and after using criteria from literature for specific conditions or Brighton Collaboration case definition guidelines where available (for AEFI classification). Criteria for causality were modified from WHO-UMC's (Uppsala Monitoring Centre) causality assessment system [11]. Outcomes for each evaluated case were classified according to whether there was recovery without sequelae, recovery with residual sequelae (e.g. disability or chronic infection), death, or unknown/lost to follow-up. All AEFIs that were categorized as Possible, Probable, or Certain (defined



**Table 1**  
Characteristics and outcomes of children admitted with suspected AEFI requiring further evaluation.

	Overall	Certain	Probable	Possible	Unlikely/unrelated
Number (n, % overall)	1988 (100%)	55 (2.8%)	53 (2.7%)	203 (10.2%)	1677 (84.4%)
Age (months; median, IQR)	3.1 (0.6–6.8)	2.1 (1.4–3)	3.9 (1.8–7.1)	3.2 (1.3–9.6)	3.1 (0.4–6.8)
Sex (male; n, % within category)	1145 (57.6%)	35 (63.6%)	37 (69.8%)	115 (56.7%)	958 (57.1%)
Race (n, % within category)					
Chinese	1028 (51.7%)	26 (47.3%)	31 (58.5%)	119 (58.6%)	852 (50.8%)
Malay	656 (33%)	16 (29.1%)	12 (22.6%)	52 (25.6%)	576 (34.3%)
Indian	156 (7.8%)	8 (14.5%)	5 (9.4%)	15 (7.4%)	128 (7.6%)
Others	148 (7.4%)	5 (9.1%)	5 (9.4%)	17 (8.4%)	121 (7.2%)
Median interval from vaccination to event onset (days; median, IQR)	6 (2–11)	58 (40–87)	90 (29–156)	9 (1–49)	5 (2–10)
Outcome (n, % within category)					
Recovered	1964 (98.8%)	54 (98.2%)	52 (98.1%)	182 (89.7%)	1676 (99.9%)
Recovered with sequelae	17 (0.8%)	1 (1.8%)	0	15 (7.4%)	1 (0.1%)
Died	1 (0.1%)	0	1 (1.9%)	0	0
Unknown/lost to follow-up	6 (0.3%)	0	0	6 (2.9%)	0

AEFI: adverse event following immunization; IQR: inter-quartile range.

as the “Possible-and-Above” group) were reported to HSA, with additional reporting for select AEFIs that may have been classified as Unlikely but were clinically significant (e.g. Bell’s palsy 4 months after vaccination, and transient urticaria post-vaccination that resolved after conservative management).

### 2.3. Statistical methods and approval

Descriptive statistics were applied to categorical and continuous data. For the “Possible-and-Above” group, we also calculated total monthly rates of AEFI per 1000 paediatric admissions, as well as monthly rates of AEFI for specific vaccines. Signal AEFI thresholds were defined by an increase of rates more than 1 standard deviation above the arithmetic mean. Data analysis was performed using SPSS version 19 software (IBM, Armonk, NY, USA). Incidence rate ratios were calculated using OpenEpi software, v3.0.1 [12]. The institutional review board of KKH approved the study.

## 3. Results

From April 2010 through March 2012, we screened 45,571 children out of 56,526 paediatric admissions (80.6%), out of which 1988 admissions (4.4%) were identified as suspected AEFI due to temporal association with recent vaccination. These were attributable to 2695 vaccines (it was not uncommon for children to receive >1 vaccine at each vaccination visit). Table 1 describes the baseline characteristics and outcomes of children admitted with suspected AEFI requiring further evaluation, while Tables 2 and 3 list the common clinical events and vaccines identified in these children. The median age at presentation was 3.1 months (inter-quartile range

(IQR), 0.6–6.8 months), while 57.6% were males. Median interval from vaccination to onset of symptoms was 6 days (IQR, 2–11 days). With regards to outcomes, 6 cases were lost to follow-up, while 98.8% fully recovered without any clinical sequelae. Seventeen patients recovered but had long-term sequelae (there were 16 children who had acquired hepatitis B infection vertically from their mothers, thus representing “vaccine failure” and life-long chronic infection, and 1 child with primary immunodeficiency had mild developmental delay following Bacillus Calmette–Guérin (BCG) meningitis), while 1 patient died (this was a child who succumbed to fulminant vaccine-type invasive pneumococcal disease despite being vaccinated with 7-valent pneumococcal conjugate vaccine (PCV) previously). Hence, except for the patient with BCG meningitis, most of the evaluated cases did not have unfavourable long-term outcomes arising directly due to an adverse event following vaccination.

There were 311 children (15.6%) with AEFI classified as “Possible-and-Above” following the receipt of 367 different vaccines, while the remaining 1677 children had events that were classified as Unlikely or Unrelated to the implicated vaccine. The most common event in the “Possible-and-Above” AEFI group was regional lymphadenitis following Bacillus Calmette–Guérin (BCG) vaccination (149 children; median interval to onset 68 days, IQR 41–102 days), followed by fever without source, commonly occurring after Hepatitis B (32 children; median interval 0 days, IQR 0–1 days) and diphtheria-tetanus-pertussis (DTP) based vaccines (18 children; median interval 1 day, IQR 0–2 days). Febrile seizures were detected more commonly after measles-mumps-rubella (MMR) vaccines (15 children; median interval to onset 7 days, IQR 4.5–8 days; median interval to onset for all febrile

**Table 2**  
Common events identified in children admitted with suspected AEFI requiring further evaluation.

Causality category	Possible-and-above				Unlikely/unrelated
	Total	Certain	Probable	Possible	
Number (n, % overall)	311 (15.6%)	55 (2.8%)	53 (2.7%)	203 (10.2%)	1677 (84.4%)
Common events identified (only listed events with >5% frequency, unless ≤6 events within category) (event; n, % within category)	Lymphadenitis (149, 47.9%)	Lymphadenitis (51, 92.7%)	Lymphadenitis (44, 83%)	Lymphadenitis (54, 26.6%)	URTI (550, 32.8%)
	Fever without source (56, 18%)	Vaccine administration site reactions (2, 3.6%)	Vaccine administration site reactions (5, 9.4%)	Fever without source (53, 26.1%)	GE & GER/vomiting (305, 18.2%)
	Seizures (34, 10.9%)	BCG meningitis (1, 1.8%)	Fever without source (3, 5.5%)	Seizures (34, 16.7%)	Fever without source (221, 13.2%)
	Kawasaki Disease (20, 6.4%)	BCG osteomyelitis (1, 1.8%)	Vaccine failure (1, 1.8%)	Kawasaki Disease (20, 9.9%)	UTI (149, 8.9%)
	Vaccine failure (16, 5.1%)			Vaccine failure (15, 7.4%)	Neonatal Jaundice (130, 7.8%)
					Seizures (99, 5.9%)

AEFI: adverse event following immunization; URTI: upper respiratory tract infection; GE: gastroenteritis; GER: gastro-esophageal reflux; BCG: Bacille–Calmette–Guérin; UTI: urinary tract infection.



**Table 3**

Common vaccines implicated in children admitted with suspected AEFI requiring further evaluation.

Causality category	Possible-and-above				Unlikely/unrelated
	Total	Certain	Probable	Possible	
No. of vaccines implicated (n, % overall)	367 (13.6%)	55 (2%)	54 (2%)	258 (9.6%)	2328 (86.4%)
Common vaccines implicated (only listed vaccines with >5% frequency, unless ≤6 events within category) (type of vaccine <sup>a</sup> ; n, % within category)	BCG (171, 46.6%) Hep B (64, 17.4%) DTP (61, 16.6%) PCV (24, 6.5%) MMR (23, 6.3%)	BCG (52, 94.5%) Hep B (2, 3.6%) DTP (1, 1.8%)	BCG (44, 81.5%) DTP (6, 11.1%) Hep B (1, 1.9%) PCV (1, 1.9%) MMR (1, 1.9%) RV (1, 1.9%)	BCG (75, 29.1%) Hep B (61, 23.6%) DTP (54, 20.9%) PCV (23, 8.9%) MMR (22, 8.5%) RV (14, 5.4%)	Hep B (807, 34.7%) DTP (564, 24.2%) BCG (451, 19.4%) PCV (230, 9.9%) MMR (131, 5.6%)

AEFI: adverse event following immunization; BCG: Bacille–Calmette–Guérin; Hep B: hepatitis B; DTP: diphtheria–tetanus–pertussis; PCV: pneumococcal conjugate vaccine; MMR: measles–mumps–rubella; RV: rotavirus vaccine.

Hep B—includes monovalent hepatitis B vaccine only;

BCG—includes BCG vaccine only;

DTP—includes diphtheria–tetanus–pertussis (3-in-1), 4-in-1 (3-in-1 combined with inactivated polio vaccine), 5-in-1 (4-in-1 combined with *Haemophilus influenzae* type b vaccine) and 6-in-1 (5-in-1 combined with hepatitis B vaccine) vaccines;

PCV—includes 7-valent, 10-valent and 13-valent conjugate vaccines;

MMR—includes MMR and MMRV vaccines (combination MMR with varicella vaccine);

RV—includes monovalent and pentavalent rotavirus vaccines.

<sup>a</sup> The types of vaccines are categorized according to the predominant component of implicated vaccines and include vaccines from different brands. Hence:

seizures after MMR vaccines regardless of causality was 7 days, IQR 4–15 days), while afebrile seizures were commonly implicated after DTP-based vaccines (9 children; median interval to onset 8 days, IQR 1–15 days). Kawasaki Disease was detected more commonly after DTP-based vaccines (9 children; median interval 9 days, IQR 5–12 days) and PCV vaccines (8 children; median interval 13 days, IQR 7–16 days), though in 5 cases the AEFI was preceded by receipt of both DTP-based and PCV vaccines. Vaccine failures were seen with hepatitis B vaccine (15 cases) and PCV (1 child). Other AEFIs occurred much more infrequently (e.g. vaccine administration site reactions, thrombocytopenia, erythema multiforme, diarrhoea, persistent crying after vaccination, Bell's palsy, myasthenia gravis, breath-holding episodes etc.), and except for intussusception following rotavirus vaccines (3 children) and BCG-associated meningitis or osteomyelitis, were not more commonly seen with any vaccine in particular.

Fig. 1 shows the trend in rates of AEFI for the “Possible-and-Above” group of children, for 5 of the most commonly implicated group of vaccines. We did not find any obvious increases in rates of AEFI following DTP, MMR or PCV based vaccines during this period (mean rates and corresponding standard deviations were  $0.97 \pm 0.66$ ,  $0.39 \pm 0.54$  and  $0.39 \pm 0.32$  events per 1000 admissions, respectively). There was a transient increase in AEFI rates following hepatitis B vaccination in February 2012 (mean rate and standard deviation of  $1.13 \pm 1.42$  events per 1000 admissions), which was explained by the fact that multiple reports of vaccine failure (which

resulted in vertical transmission of hepatitis B) that had occurred over several months had only been captured by the surveillance team that month. However, there was a gradual and significant increase in AEFI rates detected following BCG vaccination, from 0.9 events per 1000 admissions in April 2010 to 4.5 events per 1000 admissions (rate ratio 5, 95% CI 1.2–33.1; mean rate and standard deviation was  $3 \pm 1.73$  events per 1000 admissions). The most common AEFI detected following BCG vaccination was regional suppurative lymphadenitis proximal to the BCG vaccination site.

#### 4. Discussion

To our knowledge, this is the first study in the South-East Asian region describing the results of an active inpatient surveillance programme for AEFI. Our hospital based active AEFI surveillance was able to detect signals for further action, as in the case of lymphadenitis following BCG vaccination. We were able to generate stable Table 4 baseline expected rates which would enhance future options in verifying unusual signals. Our results were reassuring in that, with very few exceptions, the majority of children who were admitted to hospital within a specified risk period after recent immunization had events which were unlikely to be associated with the recent vaccine, and nearly all recovered without any significant sequelae (including those whose condition were likely to be related to the vaccine). We believe that such a system can be replicated by hospitals nationally and regionally and enhance

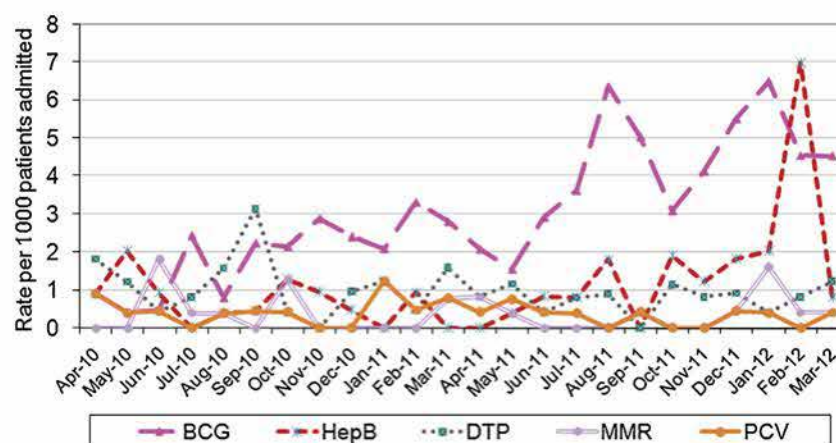


Fig. 1. Trends in rate of possible-and-above adverse events following immunization.



**Table 4**  
Common events temporally linked with implicated vaccines for children classified with “Possible-and-Above” AEFI’s.

Implicated vaccines	Most common AEFIs detected (number of children, % within category)
BCG	Lymphadenitis (149, 87.1%)
Hep B	Fever without source (33, 51.6%), Vaccine failure (15, 23.4%)
DTP	Fever without source (21, 34.4%), Afebrile seizures (9, 14.8%), Kawasaki disease (9, 14.8%)
PCV	Kawasaki disease (8, 33.3%), Fever without source (4, 16.7%), Afebrile seizures (3, 12.5%), Febrile seizures (3, 12.5%)
MMR	Febrile seizures (15, 65.2%)
RV	Intussusception (3, 20%)

AEFI: adverse event following immunization; BCG: Bacille–Calmette–Guérin; Hep B: hepatitis B; DTP: diphtheria–tetanus–pertussis; PCV: pneumococcal conjugate vaccine; MMR: measles–mumps–rubella; RV: rotavirus vaccine. Note: certain Vaccine–AEFI associations occur in the context of multiple vaccines given at the same time leading to a single AEFI, and does not necessarily imply a direct relationship. Refer to Table 3 for vaccine group categorizations.

post-marketing AEFI surveillance in this part of the world. The cost of similar surveillance systems would depend mainly on manpower costs (which would likely be lower regionally), as well as existing information technology infrastructure (which have become widespread in the region). As the region develops, maintaining public confidence in vaccine safety will become a major issue which public health bodies must manage.

With regard to AEFI that were identified as causally associated with vaccines, the most common vaccine identified in our study was that of regional lymphadenitis following BCG vaccination, and we had previously reported this briefly in a local HSA bulletin [13]. The development of lymphadenitis following BCG vaccination would usually be dependent on multiple factors which are beyond the scope of this report, but previous reports on increased incidence rates in vaccination programmes have commonly been ascribed to be due to a change in vaccine strain [14]. We have begun to undertake further analysis of the causes for the increase in incidence rates and intend to report this in future.

We did encounter several problems during the surveillance. The development of electronic data capture and analysis tools occurred incrementally, and access to hospital admissions and diagnostic data required a lengthy approval process. We obtained ethics approval for the study based on public safety and worked closely with primary physicians to capture and report AEFIs; Singapore law did not mandate notification of AEFIs except from vaccine manufacturers and in-principle consent was sought from physicians to report on their behalf in return for full access to reports. We communicated significant findings from our surveillance to physicians where clinically indicated and to HSA, except in circumstances where patient safety was an issue (e.g. when precautions were required for the next dose of the implicated vaccine or when it was contraindicated altogether), when we sought permission from primary physicians to express our findings to patients. Also, when signal thresholds were reached, the team would review and check the relevant cases again with all available and new information such as latest laboratory results etc. If the spike and possible link with vaccine(s) cannot be ruled out, HSA, the national body responsible for drug safety would be alerted. Detailed case information would be retrieved and forwarded to HSA upon request. Subsequent investigations will be led by HSA, which include correlating AEFI signals with corresponding national level diagnoses trends, discussing with vaccine manufacturers on product-quality related defects, or reviewing potential for immunization error at ground level (although detailed descriptions of these are beyond the scope of our paper).

There were several limitations to our study results. First, the use of pre-defined diagnosis and age-based criteria (Appendix 1) to identify patients who may have an AEFI could miss cases among patients with an AEFI who were not included in these criteria, although we did attempt to verify recent vaccination status for all admissions outside the above criteria. We could also have missed cases initially admitted with a diagnosis that was not within the criteria, and who then develop an AEFI of interest and have a discharge diagnosis that would reflect this; we have been working to include reviewing discharge diagnoses of interest as well. Similarly, although every attempt was made to ascertain recent vaccination data from the Health Booklet or NIR, some patients may have had a vaccine given within the implicated time frame but this was not recorded by the prescribing healthcare provider. However, this would be less likely given that providers were legally required to report childhood vaccines given as part of the Infectious Disease Act in Singapore. With regards to AEFI rates, the AEFI rates by vaccine type was calculated using hospital admissions as a denominator, although it would have been more accurate to use the total number of children vaccinated with that particular vaccine from the national registry. In addition, we would not be able to accurately assess rates in relation to changes in vaccine uptake over time or assess a vaccine given at certain times of the year (e.g. influenza). Despite this, unless there were significant changes in hospital admission patterns, we have shown that using this denominator did allow us to generate fairly stable AEFI rates over the study period, and in future we hope to be able to obtain population level vaccination data from NIR. Another limitation was that our inpatient based active AEFI surveillance would have missed cases that may have presented at outpatient or Emergency departments without being admitted. With regards to causality assessment, our descriptions of the various AEFI–vaccine combinations were based solely on the frequency with which they occurred, and were not all confirmed statistically or biologically (except perhaps for lymphadenitis following BCG vaccination); hence, while we would suggest that there were temporal associations between various vaccine and AEFI pairs, no definite conclusions can be derived regarding causality. Hence, in its present form, the surveillance merely generates baseline data and lacks evaluation of the sensitivity of the AEFI–vaccine combinations detected. Finally, due to the single-centre nature of our study, it was highly likely that there were more cases of AEFI that had been admitted to other institutions, although we attempted to adjust for this using hospital admissions as our denominator. Given the above limitations, we recognize that our rates were likely to be underestimates.

In Singapore, AEFI reporting is not mandated by law, and historically AEFI were reported together with other medicinal products to HSA. In 2007, a passive AEFI reporting system was introduced but suffered from significant limitations, especially with regard to incomplete reports (arising from poor documentation, inadequate access to laboratory or radiologic reports, and incomplete follow-up) and under-reporting, which is a common issue in other countries [15]. Anecdotal reports suggest that healthcare workers faced significant uncertainty in identifying AEFI and proving associations (after ruling out other factors) and hence were generally hesitant to report AEFI. As a result, there were very few AEFI reported prior to 2009, with ~32 reports per year reported to HSA between 2005 and 2008 (for children <18 years of age). In several other countries these limitations were partly overcome by the large number of reports received, which then permitted epidemiologic monitoring of trends. However, this was not possible in our local context until the commencement of the current active surveillance, which contributed more than 200 AEFI reports submitted to HSA within a 2-year period. We have thus shown that a hospital-based active surveillance programme can significantly augment passive AEFI surveillance. Indeed, with improved reporting, future AEFI



signals may be verified by comparing them to background event incidence rates generated from healthcare databases, also known as observed-over-expected (O/E) analysis [16,17]. This would be especially useful in situations when a new vaccine is rapidly licensed and marketed for use, for example during a pandemic. In addition, since the completion of this study, we have begun to pilot causality assessment of AEFIs using both the traditional WHO-UMC system as well as the latest WHO causality algorithm, which could aid in comparing the sensitivity of both systems [18]. We hope that continued utility of such a system would enable real-time monitoring of AEFI trends nationally, and hopefully detect AEFI signals more rapidly, thereby enhancing national vaccine safety.

### Conflict of interest statement

KCT has received funding to attend conferences from Pfizer, MSD, GSK; for speaking engagements from Pfizer, GSK; and as part of an advisory board from GSK; all these were unrelated to the submitted work. CYC has received funding from Sanofi, Pfizer and GSK to attend conferences outside the submitted work. CFY has received funding to attend a conference from Sanofi outside the submitted work. All other authors have no relevant conflicts of interest to disclose. All authors have no financial relationships relevant to this article to disclose as well.

### Contributors' statement

**Koh Cheng Thoon:** Dr. Thoon conceptualized and designed the study, collected and carried out initial analyses of the data, drafted the initial manuscript, and approved the final manuscript as submitted.

**Sally Soh:** Ms. Soh assisted in the design of the study, collected and carried out initial analyses of the data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

**Woei Kang Liew, Natalie Tan, and Chia Yin Chong:** Drs. Liew, Tan and Chong assisted in the initial analyses of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

**Arunan Gunachandran:** Mr. Gunachandran collected most of the data, assisted in the initial analyses of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

**Chee Fu Yung:** Dr. Yung assisted in the design of the study and the initial analyses of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

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writing of the report; and in the decision to submit the article for publication.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.vaccine.2014.07.020>.

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**From:** Bailey, Steven R.  
**Sent:** Wed, 26 Nov 2014 14:59:14 +0000  
**To:** Holm Karin;Antonia Utami;Arlett, Peter;Ayoub, Ayman;Bachtiar, Novilia;Benkirane (raja.benkirane@gmail.com);Blum, Michael (BlumM@MedImmune.com);Bonhoeffer, Jan (j.bonhoeffer@brightoncollaboration.org);Brigitte.Keller-Stanislawski@pei.de;Caplanusi, Irina (Irina.Caplanusi@ema.europa.eu);Ceuppens, Marc (mceuppe1@its.jnj.com);Dana, Adrian (adrian\_dana@merck.com);Darko, Mimi (mimidarko66@yahoo.co.uk);Martin, David (FDA/CBER);Dawei, Liu (liudw929@126.com);Destefano, Frank (CDC/OID/NCEZID);Dodoo, Alex UMC;Duo, Dong;Fabio Lievano (alt);Gunale, Bhagwat (alt);Hartigan-Go, Kenneth;Joan Benson (alt) (joan\_benson@merck.com);Jouquelet-Royer, Corinne;Kulkarni, Prasad;Lindquist, Marie;Maure, Christine;Mentzer, Dirk;'Nishioka, Sergio';Nohynek Anna (Hanna.Nohynek@thl.fi);Oberle, Doris (alt2);Owden Amanda;PatelMayur@MedImmune.com;Paulo.santos@bio.fiocruz.br;Peter Glen Y. Chua (peterchuamd@gmail.com);Ramkishan, Ajmeer;Rauscher, Martina;Rmenezes@bio.fiocruz.br;Seifert, Harry;Shimabukuro, Tom (CDC/OID/NCEZID);Sillan, Françoise;Siti Asfijah Abdoellah (alt);Sjolin\_Forsberg Gunilla;sten.olsson@who-umc.org;swati srivastava (alt);Tebaa, Amina;terhi.kilpi@thl.fi;Bergman Ulf;ulrich.heininger@ukbb.ch;Gregory, William (NYC);Winiacki, Scott (FDA/CBER);Xavier.Kurz@ema.europa.eu;Youssef, Mona (b)(6) Zuber, Patrick (CDC who.int)  
**Cc:** Ingemar Persson (ingemarpersson@me.com)  
**Subject:** RE: CIOMS Vaccine Safety TC by WHO for Friday 21 November 15h-16h (3-4 pm) Geneva Time  
**Attachments:** Ch1-IP-draftV1-141125.docx  
**Importance:** High

All:

As most of you are aware, in Rabat we agreed to re-order the document a bit, taking some points covered by TG2 and expanding them, and putting them up front. This led to the creation of two new chapters, number 1 and 2.

For Chapter 1, Corinne, Irina and myself agreed to draft the outline, with formal review by Scott and Sergio. Thanks to the hard work of this group, we were able to complete this ahead of schedule.

Even better, we were able to take advantage of Ingemar's availability to turn this outline into a first draft of the chapter. His draft is attached (and is excellent: thank you Ingemar!)

As agreed in Rabat, it is critical that this chapter contain examples, and we thought it would be important to get a wide variety of examples from various regions and stakeholders. Therefore, we are requesting the entire group to suggest and provide pertinent examples. If you look through the document (esp. the latter portion, page 4 onward), you will see highlighted placeholder for example.

We kindly request that anyone who can provide pertinent example to do so, in as timely a manner as you can. With these examples in place, we will have a very solid first draft of this important chapter, and can then move forward with review and updates to it, and eventually full team discussion in Lyons.

Please ensure that at minimum Ingemar, Corinne, Irina, Sergio, Scott, Karin and myself are included when you forward you example.

Many thanks to all,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

(b)(5)



(b)(5)

(b)(5)

(b)(5)

(b)(5)

(b)(5)

**From:** Corinne.Jouquelet-Royer@sanofipasteur.com  
**Sent:** Mon, 18 Aug 2014 13:33:34 +0000  
**To:** terhikilpi@thl.fi; BlumM@MedImmune.com; Steven.R.Bailey@pfizer.com; Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** maurec@who.int; holmk@cioms.ch; Françoise.Sillan@sanofipasteur.com  
**Subject:** CIOMS/WHO TG2 Section 5.3  
**Attachments:** CIOMS TG2 business plan TG2\_18july\_fs-cgm.docx

Dear Michael, Steve, Frank and Tehri,

(b)(4)

Terhi has kindly accepted to contribute to section 5.3 and was wondering if you, the 3 gentlemen, would be happy to contribute.

As a reminder: a high level draft is expected by Sept 3.

Thank you

Best regards

Co

**Dr Corinne Jouquelet-Royer**

Vice President Global Pharmacovigilance

TEL.: +33 (0)4.37.66.97.47 - CELL.: +33 (0)6.32.04.99.97

SIÈGE MONDIAL - 2, AVENUE PONT PASTEUR - 69367 LYON cedex 07 - France

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(b)(4)



**From:** Bailey, Steven R.  
**Sent:** Thu, 28 Aug 2014 18:28:41 +0000  
**To:** Holm Karin;Caplanusi Irina;Corinne.Jouquelet-Royer@sanofipasteur.com;Harry.A.Seifert@gsk.com;Francoise.Sillan@sanofipasteur.com;mimidarko66@yahoo.co.uk;Zuber, Patrick (CDC who.int);maurec@who.int;Winiecki, Scott (FDA/CBER);terhi.kilpi@thl.fi;novilia@biofarma.co.id;Destefano, Frank (CDC/OID/NCEZID);liudw929@126.com;Kurz Xavier;Martin, David (FDA/CBER);Bergman Ulf;dongduo@cdr.gov.cn;BlumM@MedImmune.com  
**Cc:** Sjolín\_Forsberg Gunilla  
**Subject:** RE: Draft 5a - Chapter 5, CIOMS Vaccine Safety TG2  
**Attachments:** holmk\_Draft chapter 5a srb.docx

All:

I have added some comments to this draft (comments only: and merely suggestion). All items that could be discussed in Rabat.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** Thursday, August 21, 2014 9:34 AM  
**To:** Caplanusi Irina; Corinne.Jouquelet-Royer@sanofipasteur.com; Harry.A.Seifert@gsk.com; Francoise.Sillan@sanofipasteur.com; (b)(6); zuberp@who.int; maurec@who.int; Scott.Winiecki@fda.hhs.gov; terhi.kilpi@thl.fi; novilia@biofarma.co.id; fxd1@cdc.gov; liudw929@126.com; Kurz Xavier; David.Martin@fda.hhs.gov; Bergman Ulf; Bailey, Steven R.; dongduo@cdr.gov.cn; BlumM@MedImmune.com  
**Cc:** Sjolín\_Forsberg Gunilla  
**Subject:** Draft 5a - Chapter 5, CIOMS Vaccine Safety TG2

Dear Corinne, Irina, et al.

I found this draft to be an excellent overview of purpose, well-documented, and very understandable, even for a non-vaccine expert like myself. Attached just minor suggestions and question in the attached file.

Karin

---

**Karin R. Holm**

Publications Consultant, WG IX Risk Minimisation  
Technical Coordinator, WG on Vaccine Safety  
Council for International Organizations of Medical Sciences (CIOMS)

Associate partner of UNESCO and in official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland  
Ofc Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)  
Email: [holm@cioms.ch](mailto:holm@cioms.ch)

---

**From:** Caplanusi Irina [[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)]  
**Sent:** 05 August 2014 10:46  
**To:** Holm Karin; [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); [REDACTED]; [zuberp@who.int](mailto:zuberp@who.int); [maurec@who.int](mailto:maurec@who.int); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [liudw929@126.com](mailto:liudw929@126.com); Kurz Xavier; [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; [Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)  
**Subject:** RE: Reminder - Chapter 5, CIOMS Vaccine Safety TG2

Dear CIOMS WG on Vaccine Safety – TG 2, chapter 5

Please find enclosed the draft chapter 5a that Xavier, David and me have prepared as a working document to start the discussion.

Kind regards,  
Irina

---

**From:** Holm Karin [<mailto:holm@cioms.ch>]  
**Sent:** 01 August 2014 15:35  
**To:** [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [zuberp@who.int](mailto:zuberp@who.int); [maurec@who.int](mailto:maurec@who.int); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [liudw929@126.com](mailto:liudw929@126.com); Kurz Xavier; Caplanusi Irina; [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; [Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)  
**Cc:** [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); [REDACTED] (b)(6)  
**Subject:** Reminder - Chapter 5, CIOMS Vaccine Safety TG2

Dear CIOMS WG on Vaccine Safety -- Topic group 2, chapter 5

We hope you can devote some time over next weeks to developing your section of chapter 5.

Dates to work on:

Thurs. 21 August - progress report to Corinne and Harry on your section.

Wed. 3 Sept - draft of your section due to Corinne and Harry.

Tues. 9 Sept, 1pm (Lyon France) - TeleConference to prepare for Rabat (best date from doodle poll).

See attached for latest action plan and key steps from Corinne.  
Karin

---

**Karin R. Holm**

Publications Consultant, WG IX Risk Minimisation

Technical Coordinator, WG on Vaccine Safety

Council for International Organizations of Medical Sciences (CIOMS)

Associate partner of UNESCO and in official relations with WHO

c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland



Ofc Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)

Email: [holm@cioms.ch](mailto:holm@cioms.ch)

---

**From:** [Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com) [Corinne.Jouquelet-Royer@sanofipasteur.com]

**Sent:** 31 July 2014 11:16

**To:** Holm Karin; [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); [zuberp@who.int](mailto:zuberp@who.int); [maurec@who.int](mailto:maurec@who.int); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [liudw929@126.com](mailto:liudw929@126.com); [Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; [Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); [BlumM@MedImmune.com](mailto:BlumM@MedImmune.com)

**Cc:** [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); (b)(6)

**Subject:** RE: CIOMS WG on VS TG2 chapter 5

Dear all,

As agree you will find attached the result of the literature search. The search criteria included:

Pharmacovigilance

Safety . side effects. Adverse events

Monitoring

Post marketing

Observational study

Vaccine

Surveillance, active surveillance , passive surveillance

Network

LMIC (Low Middle Income Countries)

Feel free to add any reference when writing your section.

Kind regards

Co

---

**From:** Holm Karin [<mailto:holm@cioms.ch>]

**Sent:** samedi 5 juillet 2014 21:37

**To:** Jouquelet-Royer, Corinne (sanofi pasteur); [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); Patrick Zuber ([zuberp@who.int](mailto:zuberp@who.int)); [maurec@who.int](mailto:maurec@who.int); Winiecki, Scott; [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); Bachtiar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); [Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu); Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; Bailey ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com)); [dongduo@cdr.gov.cn](mailto:dongduo@cdr.gov.cn); Blum, Michael ([BlumM@MedImmune.com](mailto:BlumM@MedImmune.com))

**Cc:** Sillan, Francoise (sanofi pasteur); Darko, Mimi ( (b)(6) )

**Subject:** RE: CIOMS WG on VS TG2 chapter 5

Dear Contributors to TG2 Chapter 5,

Additional contributors are needed, especially for section 5.2 and 5.4 --- for the later the public sector is key actor and also a regulator.

For the next TC, I am sending a doodle poll for 1.5 hour on the 8 , 9 or 10 of September in the afternoon.

Please note that Corinne and Harry need your drafts by September 3.

Please note that I am on vacation 7-28 July with only limited access to computers.

Best regards,  
Karin

---

**Karin R. Holm**

Publications Consultant, WG IX Risk Minimisation

Technical Coordinator, WG on Vaccine Safety

Council for International Organizations of Medical Sciences (CIOMS)

Associate partner of UNESCO and in official relations with WHO

c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland

Ofc Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)

Email: [holm@cioms.ch](mailto:holm@cioms.ch)

---

**From:** Holm Karin

**Sent:** 24 June 2014 11:36

**To:** Jouquelet-Royer, Corinne; [Harry.A.Seifert@gsk.com](mailto:Harry.A.Seifert@gsk.com); Patrick Zuber ([zuberp@who.int](mailto:zuberp@who.int)); [maurec@who.int](mailto:maurec@who.int); Winiecki, Scott; [terhi.kilpi@thl.fi](mailto:terhi.kilpi@thl.fi); Bachtiar ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); [fxd1@cdc.gov](mailto:fxd1@cdc.gov); Dawei, Liu ([liudw929@126.com](mailto:liudw929@126.com)); [Xavier.Kurz@ema.europa.eu](mailto:Xavier.Kurz@ema.europa.eu); Caplanusi, Irina ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); [David.Martin@fda.hhs.gov](mailto:David.Martin@fda.hhs.gov); Bergman Ulf; Bailey ([Steven.R.Bailey@pfizer.com](mailto:Steven.R.Bailey@pfizer.com))

**Cc:** [Francoise.Sillan@sanofipasteur.com](mailto:Francoise.Sillan@sanofipasteur.com); Darko, Mimi ( (b)(6) )

**Subject:** CIOMS WG on VS TG2 section 5 - Fri 27 June 12noon (French time)

Dear CIOMS TG2 Chapter 5 Contributors,

Corinne Jouquelet-Royer (Sanofi, who is new to the CIOMS WG but will eventually take over at some point in the future for Françoise, who is moving to a new area at Sanofi) and Harry Seifert (GSK) kindly offered to organize Chapter 5 of the Manual on Active Safety Surveillance. Ch.5 is the "meat of the manual" on Establishing Active Surveillance (see Table of Contents in business plan draft attached).

The best day/time was this Friday, 27 June, 12pm French time. Sanofi kindly will arrange TC and send instructions on how to access.

**Agenda for TC**

- Quick review of the section 5 to get alignment and shared understanding on what need to be achieved
- Agree on contributors to which sections
- And timelines for draft and reviews before September meeting

June

2014

Fri 27

	12:00 PM
Karin Holm	NO
corinne jouquelet royer	OK
Harry Seifert	OK
Patrick Zuber	OK
Christine Maure	OK
Scott Winiecki (FDA)	OK
Frank DeStefano	NO
Terhi Kilpi	OK
Novilia Sjafri Bachtar	OK
Xavier Kurz	OK
Dawei Liu	?
Irina Caplanusi	?
David Martin	?
Steven Bailey	?
Ulf Bergman	NO
Count	8

**Karin R. Holm**

Technical Coordinator, Working Group on Vaccine Safety

Publications Consultant, Working Group IX Risk Minimization

Council for International Organizations of Medical Sciences (CIOMS)

Associate partner of UNESCO / In official relations with WHO

c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland

Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)

Email: [holmkr@cioms.ch](mailto:holmkr@cioms.ch)

---

This e-mail has been scanned for all known viruses by European Medicines Agency.

---

(b)(4)

(b)(4)

(b)(4)



**From:** Francoise.Sillan@sanofipasteur.com  
**Sent:** Wed, 21 May 2014 09:07:39 +0000  
**To:** Steven.R.Bailey@pfizer.com;novilia@biofarma.co.id;holmk@cioms.ch;atebaa@yahoo.fr;mimidarko66@yahoo.co.uk;Destefano, Frank (CDC/OID/NCEZID);maurec@who.int;Harry.A.Seifert@gsk.com;sjolinforsbergg@cioms.ch;sten.olsson@who-umc.org;Destefano, Frank (CDC/OID/NCEZID);holmk@cioms.ch  
**Subject:** summary of our discussions yesterday  
**Attachments:** Table of Content TG2-May 20.docx

Dear all  
We have summarized with Franck our discussions from yesterday in the TOC of our manual. This will be used for the debrief today

Best regards / Bien cordialement,

Françoise

-----Message d'origine-----

De : Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]

Envoyé : mercredi 21 mai 2014 09:38

À : Sillan, Francoise (sanofi pasteur); novilia@biofarma.co.id; holmk@cioms.ch; (b)(6)

(b)(6) fxd1@cdc.gov; maurec@who.int; Harry.A.Seifert@gsk.com;

sjolinforsbergg@cioms.ch; sten.olsson@who-umc.org

Objet : RE: RACI Table~TG2

Some additional thoughts/comments for discussion when we have a chance to meet.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory Global Established Pharma Safety Lead Pfizer  
484 865 3670

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

From: Francoise.Sillan@sanofipasteur.com [<mailto:Francoise.Sillan@sanofipasteur.com>]

Sent: Wednesday, May 21, 2014 3:07 AM

To: novilia@biofarma.co.id; holmk@cioms.ch; (b)(6) Bailey, Steven R.; (b)(6)

fxdl@cdc.gov; maurec@who.int; Harry.A.Seifert@gsk.com; sjolinforsbergg@cioms.ch; sten.olsson@who-umc.org

Subject: RE: RACI Table~TG2

Thank you Novilla

I have corrected the table as my poor writing led to some errors ( (b)(4)

(b)(4)

Thank you for your review and comments

Best regards / Bien cordialement,

Françoise

-----Message d'origine-----

De : Novilia [<mailto:novilia@biofarma.co.id>] Envoyé : mardi 20 mai 2014 23:34 À : Holm Karin; Amina TEBA; Bailey (Steven.R.Bailey@pfizer.com); Darko Delese, Mimi (b)(6)@cdc.gov; maurec@who.int; Harry.A.Seifert@gsk.com; Sillan, Françoise (sanofi pasteur); Sjolín\_Forsberg Gunilla; Sten Olsson (alt) Objet : RACI Table~TG2

Dear all,

Here with the RACI table which has been discussed today in TG2. Please feel free to review it. I think I already included all points recorded by Françoise and mine.

I am sorry, I don't have Dr.Fabien email address.

Best regards,  
Novi

\*\*\*\*\*

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(b)(4)

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(b)(4)

(b)(4)



**From:** Francoise.Sillan@sanofipasteur.com  
**Sent:** Tue, 21 Jan 2014 11:05:31 +0000  
**To:** holmk@cioms.ch; Destefano, Frank  
(CDC/OID/NCEZID); ulf.bergman@karolinska.se; maurec@who.int; terhi.kilpi@thl.fi; (b)(6) Dirk  
.Mentzer@pei.de  
**Subject:** RE: DRAFT Summary TC Briefing -- TG2

Dear all

Thank you Karin for the quick response

I have expanded a little bit on Karin's summary. Please feel free to add or correct as necessary.

*Best regards / Bien cordialement,*

*Françoise*

---

**De :** Holm Karin [mailto:holmk@cioms.ch]

**Envoyé :** lundi 20 janvier 2014 15:37

**À :** Sillan, Francoise (sanofi pasteur); 'Frank DeStefano (alt)'; ulf.bergman@karolinska.se; maurec@who.int; 'Terhi Kilpi'; (b)(6); Dirk Mentzer

**Objet :** DRAFT Summary TC Briefing -- TG2

DRAFT Summary TC Briefing -- TG2 "Improvement of Post-Marketing Surveillance Programmes"

20 January 2014, 14 :00 (France Time - arranged by Sanofi-Pasteur).

Topic: preparing for 3rd meeting in Atlanta

Attending: Françoise, Mimi, Frank Destefano, Christine Maure, Terhi Kilpi, Ulf Bergman, Karin

Regrets: Amina Tebaa, Dirk Mentzer

Led by Françoise Sillan (Sanofi-Pasteur) et Mimi Darko (Ghana FDA)

(b)(4)

For our meeting in Atlanta, we will create a **powerpoint presentation** to use for break-out group in afternoon of first day to discuss this idea for a main product. The powerpoint will summarize this discussion and prepare the Draft a **Table of Contents** for what the manual would look like.



At Atlanta we will work on a **business plan**, to include the delegation of assignments, tasks, activities, resources, timeline needed.

Please add, correct, expand

Deadline: Your comments by tomorrow tues 21Jan.

Deadline: I return expanded briefing by wed 22jan and return to you.

If Françoise and Mimi say it is okay, I would then distribute the briefing to the whole WG.

Deadline: powerpoint presentation to submit to me by 27january to send to CDC (I am hopeful we can do more in Atlanta but not sure. Here is what they say in their info: **Wi-Fi is available in the CDC buildings but laptops cannot be used for presentations. These must be sent two weeks in advance in order to have them uploaded to the CDC system by a technician.**)

Thank you!

Best, Karin

Karin R. Holm  
Technical Coordinator, Working Group on Vaccine Safety  
Publications Consultant, Working Group IX Risk Minimization  
Council for International Organizations of Medical Sciences (CIOMS)  
c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland  
Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)  
Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)  
(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)

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\*\*\*\*\*

**From:** Bailey, Steven R.  
**Sent:** Wed, 21 May 2014 07:37:43 +0000  
**To:** Francoise.Sillan@sanofipasteur.com;novilia@biofarma.co.id;holmk@cioms.ch;ate (b)(6);mimida  
rko66@yahoo.co.uk;Destefano, Frank  
(CDC/OID/NCEZID);maurec@who.int;Harry.A.Seifert@gsk.com;sjolinforsbergg@cioms.ch;sten.olsson@  
who-umc.org  
**Subject:** RE: RACI Table~TG2  
**Attachments:** RACI TableTG2 srb.docx

Some additional thoughts/comments for discussion when we have a chance to meet.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
Global Established Pharma Safety Lead  
Pfizer  
484 865 3670

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

From: Francoise.Sillan@sanofipasteur.com [<mailto:Francoise.Sillan@sanofipasteur.com>]  
Sent: Wednesday, May 21, 2014 3:07 AM  
To: novilia@biofarma.co.id; holmk@cioms.ch; atebaa@yahoo.fr; Bailey, Steven R. (b)(6)  
fxdl@cdc.gov; maurec@who.int; Harry.A.Seifert@gsk.com; sjolinforsbergg@cioms.ch; sten.olsson@who-umc.org  
Subject: RE: RACI Table~TG2

Thank you Novilla

I have corrected the table as my poor writing led to some errors (vaccine manufacturers replaced by vaccine managers).

Thank you for your review and comments

Best regards / Bien cordialement,

Françoise

-----Message d'origine-----

De : Novilia [<mailto:novilia@biofarma.co.id>] Envoyé : mardi 20 mai 2014 23:34 À : Holm Karin; Amina TEBA; Bailey (Steven.R.Bailey@pfizer.com); Darko Delese, Mimi (b)(6)dl@cdc.gov; maurec@who.int; Harry.A.Seifert@gsk.com; Sillan, Francoise (sanofi pasteur); Sjolin\_Forsberg Gunilla; Sten Olsson (alt) Objet : RACI Table~TG2

Dear all,

Here with the RACI table which has been discussed today in TG2. Please feel free to review it. I think I already included all points recorded by Francoise and mine.

I am sorry, I don't have Dr.Fabien email address.

Best regards,

Novi

\*\*\*\*\*

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\*\*\*\*\*

(b)(4)

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

**Claudia:**

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

You have her e-mail address (up above) and her office phone is 484-865-5950. Please don't hesitate to call her.

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

Thanks again,  
Gregg

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

---

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

Gregg

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

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

---

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

**Claudia:**

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



I was wondering if your team (internal/external) has finished the

(b)(4)

(b)(4)

(b)(4) If not.....do you know when it might be finished?

Thanks,  
Gregg

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

---

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

That shouldn't be problem  
Claudia

---

**From:** Sylvester, Gregg C [<mailto:Gregg.C.Sylvester@pfizer.com>]  
**Sent:** Wednesday, April 18, 2012 5:41 PM  
**To:** Vellozzi, Claudia (CDC/OID/NCEZID)  
**Cc:** Destefano, Frank (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID)  
**Subject:** RE: Pfizer (PCV13) Safety

Claudia:

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

(b)(4)

Thanks again,  
Gregg

---

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

Hi Gregg,  
I just wanted you to know that I did discuss this with our counterparts at the FDA (so not Holly below) and they will share our update regarding the timeline for a (b)(4)  
I hope this helps.  
Thanks,

Claudia

---

**From:** Sylvester, Gregg C [<mailto:Gregg.C.Sylvester@pfizer.com>]  
**Sent:** Wednesday, April 11, 2012 9:59 AM  
**To:** Vellozzi, Claudia (CDC/OID/NCEZID); Shimabukuro, Tom (CDC/OID/NCEZID)  
**Subject:** RE: Pfizer (PCV13) Safety

**Claudia & Tom:**

Holly Wieland (301-796-2640) is the person that we had spoken to at CBER within the FDA. Please don't hesitate to tell her that you have spoken with us. (b)(4)

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

(b)(4)

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

Thanks you,  
Gregg

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

---

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

Gregg,

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

Thanks.

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

---

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

Okay, thanks.  
Tom

---

**From:** Sylvester, Gregg C [<mailto:Gregg.C.Sylvester@pfizer.com>]  
**Sent:** Monday, April 09, 2012 3:00 PM  
**To:** Shimabukuro, Tom (CDC/OID/NCEZID)  
**Subject:** RE: Pfizer (PCV13) Safety

**Tom & Claudia:**

Thanks again for speaking with me last week. I understand that it's too soon to sit down and share with us the results from (b)(4) however, I do want to accept your offer of talking with the FDA.

I have discussed it with my colleagues at Pfizer (b)(4)

(b)(4)

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

Thanks again,  
Gregg

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

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

---

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

Gregg,

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

Tom

---

**From:** Sylvester, Gregg C [<mailto:Gregg.C.Sylvester@pfizer.com>]  
**Sent:** Thursday, April 05, 2012 1:52 PM  
**To:** Shimabukuro, Tom (CDC/OID/NCEZID)  
**Subject:** RE: Pfizer (PCV13) Safety

**Tom:**



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

Gregg

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

---

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

Gregg,

The VSD evaluation of the association between (b)(4) is ongoing, but close to completion and we should have final results either later this month or in May. We can do a briefing for the Pfizer staff to present the final data. Maybe we can tentatively schedule something for early May. Will that work for you? Let me know.

Tom

---

**From:** Sylvester, Gregg C [<mailto:Gregg.C.Sylvester@pfizer.com>]  
**Sent:** Thursday, April 05, 2012 9:55 AM  
**To:** Shimabukuro, Tom (CDC/OID/NCEZID)  
**Subject:** RE: Pfizer (PCV13) Safety

Thank you very much.....

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

---

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

Gregg,

I am aware of the ongoing PCV13 surveillance in VSD, but not familiar with the details for (b)(4). Let me check with the VSD team and get back to you on that.

Tom

---

**From:** Sylvester, Gregg C [<mailto:Gregg.C.Sylvester@pfizer.com>]  
**Sent:** Thursday, April 05, 2012 7:54 AM  
**To:** Shimabukuro, Tom (CDC/OID/NCEZID)  
**Subject:** RE: Pfizer (PCV13) Safety

**Tom:**

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

I was actually calling you about another issue. FDA mentioned that the CDC saw a [redacted] (b)(4)

[redacted] (b)(4)  
[redacted] (b)(4) Can you direct me to the right person to discuss this matter?

**Gregg**

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

---

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

Gregg,

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

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

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

Tom

**Tom Shimabukuro, MD, MPH, MBA**  
CDR, U.S. Public Health Service

Senior Medical Officer  
Immunization Safety Office  
Centers for Disease Control and Prevention (CDC)  
1600 Clifton Road, MS D-26, Atlanta, GA 30333

Phone: 404-639-4848

Fax: 404-639-8834

Email: [TShimabukuro@cdc.gov](mailto:TShimabukuro@cdc.gov)

---

**From:** Sylvester, Gregg C [\[mailto:Gregg.C.Sylvester@pfizer.com\]](mailto:Gregg.C.Sylvester@pfizer.com)

**Sent:** Wednesday, April 04, 2012 11:22 AM

**To:** Shimabukuro, Tom (CDC/OID/NCEZID)

**Subject:** Pfizer (PCV13) Safety

**Tom:**

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

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

**Could we chat for a few minutes today?**

**Thanks,  
Gregg**

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

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

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

Dear Frank,

(b)(4)

All the best,

Guillermo Herrera Taracena, MD, MBA  
GlaxoSmithKline  
Medical Affairs  
Director Influenza Vaccines  
Tel: 610 787 3267  
Mob: 484 682 9153  
Fax: 610 787 7055

**From:** Harry Seifert  
**Sent:** Mon, 2 Mar 2015 17:53:55 +0000  
**To:** Martin, David (FDA/CBER);Nguyen, Michael D. (FDA/CBER);Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Greg Powell  
**Subject:** GSK social listening slides  
**Attachments:** FDA slides March 2015 final.ppt

Dear David, Michael, and Frank,

Attached are the slides that GSK will present at the meeting with the FDA data mining task force on Wednesday. The vaccine slides are #15-19. Although these should not be publically disclosed, you may share them freely within your organizations.

I would be happy to discuss the content of the slides, or GSK's project, or GSK's plans with you, either by phone or in person.

Best regards,  
Harry

Harry Seifert, MD, MSCE  
Executive Director  
Vaccine Clinical Safety & Pharmacovigilance  
GlaxoSmithKline Biologicals  
2301 Renaissance Blvd.  
Mail Code RN-0220  
King of Prussia, PA 19406  
USA

Email: [harry.a.seifert@gsk.com](mailto:harry.a.seifert@gsk.com)  
Office: +1 610 917 4177  
Fax: +1 610 787 7055





# **Social Listening and Post-Marketing Safety Surveillance:**

## **The Beginning**

March 2015

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(b)(4)



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(b)(4)

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# Questions

**From:** Leonard Friedland  
**Sent:** Tue, 3 Mar 2015 13:09:03 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** GSK - transaction with Novartis

Dear Dr. DeStefano,

I want to share some important news about the future of our company and, in particular, of our global vaccines business.

As you may have heard, today GSK announced the conclusion of its three-part transaction with Novartis involving the Consumer Healthcare, Vaccines and Oncology businesses.

The acquisition of Novartis' global vaccines business (excluding influenza vaccines<sup>[1]</sup>) provides GSK with an exciting opportunity to build an even stronger, sustainable global vaccines business while remaining true to our commitments to access, innovation, quality and collaboration.

The transaction will enhance our vaccines portfolio and strengthen our presence around the world, enabling us to deliver more vaccines where they are needed. It will bring together our expertise in virology, bacterial infection and technological platforms, to drive innovation in areas of unmet medical need. And it will strengthen our manufacturing network and capacity, increasing our ability to deliver a reliable supply of high quality vaccines.

We are currently working to complete the integration as quickly and as smoothly as possible and to maintain 'business as usual' wherever we can. With that in mind, I would like to confirm that I will remain your key contact for medical vaccine topics.

Dr. DeStefano, please feel free to distribute this letter to CDC Immunization Safety Office staff.

I look forward to keeping you informed as we move forward. In the meantime, if you have any questions, please don't hesitate to let me know.

With kind regards,  
Len

Leonard Friedland, MD  
VP, Scientific Affairs and Public Health  
Vaccines, North America  
GSK  
[Leonard.R.Friedland@gsk.com](mailto:Leonard.R.Friedland@gsk.com)  
484 620 9540



<sup>[1]</sup> Except in China.

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<sup>[1]</sup> Except in China.

**From:** Harry Seifert  
**Sent:** Fri, 13 Mar 2015 11:45:15 +0000  
**To:** Nguyen, Michael D. (FDA/CBER);Martin, David (FDA/CBER);Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Greg Powell  
**Subject:** RE: GSK social listening slides

All,

We were invited to return to White Oak to present again in early summer. By then, we will have actual data for the vaccine pilot explorations. I'll keep you in the loop for that presentation, too, and our offer to meet with you stands.

As a sneak peek and reassurance: Our superficial look at the data for the GSK-trade name vaccines, on Facebook and Twitter, revealed very few public posts (over the past 2 years) and no signals.

Best regards,  
Harry

Harry Seifert, MD, MSCE  
Executive Director  
Vaccine Clinical Safety & Pharmacovigilance  
GlaxoSmithKline Biologicals  
2301 Renaissance Blvd.  
Mail Code RN-0220  
King of Prussia, PA 19406  
USA

Email: [harry.a.seifert@gsk.com](mailto:harry.a.seifert@gsk.com)  
Office: +1 610 917 4177  
Fax: +1 610 787 7055

---

**From:** Nguyen, Michael D. [<mailto:Michael.Nguyen@fda.hhs.gov>]  
**Sent:** Monday, March 02, 2015 2:50 PM  
**To:** Harry Seifert; Martin, David; Destefano, Frank (CDC)  
**Cc:** Greg Powell  
**Subject:** RE: GSK social listening slides

Thank you. I was not aware that GSK was engaging in this type of work. Michael

---

**From:** Harry Seifert [<mailto:Harry.A.Seifert@gsk.com>]  
**Sent:** Monday, March 02, 2015 12:54 PM  
**To:** Martin, David; Nguyen, Michael D.; Destefano, Frank (CDC)  
**Cc:** Greg Powell  
**Subject:** GSK social listening slides

Dear David, Michael, and Frank,

Attached are the slides that GSK will present at the meeting with the FDA data mining task force on Wednesday. The vaccine slides are #15-19. Although these should not be publically disclosed, you may share them freely within your organizations.

I would be happy to discuss the content of the slides, or GSK's project, or GSK's plans with you, either by phone or in person.

Best regards,  
Harry

Harry Seifert, MD, MSCE  
Executive Director  
Vaccine Clinical Safety & Pharmacovigilance  
GlaxoSmithKline Biologicals  
2301 Renaissance Blvd.  
Mail Code RN-0220  
King of Prussia, PA 19406  
USA

Email: [harry.a.seifert@gsk.com](mailto:harry.a.seifert@gsk.com)  
Office: +1 610 917 4177  
Fax: +1 610 787 7055

**From:** Kuter, Barbara J.  
**Sent:** Tue, 14 Jan 2014 15:17:48 -0500  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: NEJM Publications

Thanks, Frank. Any info the Comms group could send along would be a help.

And congrats to your team on another excellent publication.

I will see you at the Feb ACIP meeting.

Thanks again.

Barb

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Tuesday, January 14, 2014 2:48 PM  
**To:** Kuter, Barbara J.  
**Subject:** RE: NEJM Publications

Barb,  
I will contact our communications group about sharing the talking points, but they are pretty much the same as what we used in June for the ACIP presentations.  
Frank

---

**From:** Kuter, Barbara J. [mailto:[barbara\\_kuter@merck.com](mailto:barbara_kuter@merck.com)]  
**Sent:** Tuesday, January 14, 2014 1:58 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** NEJM Publications

Hi Frank,

Happy New Year! I hope you had a relaxing holiday.

I wanted to let you know that we were a bit surprised to learn of the 3 NEJM publications today. We have had a few media requests already and so we were wondering if CDC has developed any talking points or Q & A to support these publications. If so, could you please send them along.

Many thanks.



Barb

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



**From:** Leonard Friedland  
**Sent:** Fri, 17 Jan 2014 14:45:08 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: question from GSK: NEJM Weintraub 2014 publication

Frank, thank you  
Len

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Friday, January 17, 2014 9:43 AM  
**To:** Leonard Friedland; Weintraub, Eric (CDC/OID/NCEZID)  
**Cc:** Dominique Rosillon  
**Subject:** RE: question from GSK: NEJM Weintraub 2014 publication

Len and Dominique,  
I am referring your question to Eric Weintraub, the first author and primary analyst on the manuscript. The comparison of RV1 and RV5 was based on Brighton chart-confirmed cases. Eric will be better able to address if you may be able to use the chart-confirmed cases in your meta-analysis.  
Thanks,  
Frank

---

**From:** Leonard Friedland [mailto:[Leonard.R.Friedland@gsk.com](mailto:Leonard.R.Friedland@gsk.com)]  
**Sent:** Friday, January 17, 2014 9:29 AM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Dominique Rosillon  
**Subject:** question from GSK: NEJM Weintraub 2014 publication

Dear Dr. DeStefano

(b)(4)

(b)(4)

Thank you very much,  
Len and Dominique

Leonard Friedland, MD, Scientific Affairs and Public Health  
Dominique Rosillon, Ph.D., Epidemiology – Statistics  
GlaxoSmithKline

**From:** Leonard Friedland  
**Sent:** Fri, 7 Jun 2013 20:30:59 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** RE: Rotarix VSD Intussusception data

Thank you. Is it possible for me to give you a call to discuss the reason for the request to speak to high level VSD results to health authorities?

Sincerely, Leonard Friedland

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Friday, June 07, 2013 4:23 PM  
**To:** Leonard Friedland  
**Cc:** Cortese, Margaret (CDC/OID/NCIRD); Weintraub, Eric (CDC/OID/NCEZID)  
**Subject:** RE: Rotarix VSD Intussusception data

Dear Dr. Friedland,

(b)(4)

Sincerely,

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA

---

**From:** Leonard Friedland [mailto:[Leonard.R.Friedland@gsk.com](mailto:Leonard.R.Friedland@gsk.com)]  
**Sent:** Wednesday, June 05, 2013 4:30 PM  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Cortese, Margaret (CDC/OID/NCIRD)  
**Subject:** RE: Rotarix VSD Intussusception data

Dear Dr. Destefano,

(b)(4)

Sincerely,

Leonard Friedland, MD  
Scientific Affairs and Public Policy  
GlaxoSmithKline Vaccines  
484.620.9540 (mobile)  
[Leonard.R.Friedland@gsk.com](mailto:Leonard.R.Friedland@gsk.com)

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Friday, May 03, 2013 10:02 AM  
**To:** Remon Roskoaf Abu-Elyazeed  
**Cc:** Cortese, Margaret (CDC/OID/NCIRD)  
**Subject:** Intussusception data

Dear Dr. Abu-Elyazeed:

Margaret informed me that you were interested in the topic of rotavirus vaccines and intussusception scheduled for an upcoming ACIP meeting. One of the presentations at that session will be findings from our Vaccine Safety Datalink on Rotarix and intussusception. We could provide a confidential preview to you and a limited number of other GSK staff if you are interested.

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention

Atlanta, GA

**From:** Leonard Friedland  
**Sent:** Fri, 7 Jun 2013 16:38:10 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Cortese, Margaret (CDC/OID/NCIRD)  
**Subject:** RE: Rotarix VSD Intussusception data

Dear Dr. Destefano,

(b)(4)

Sincerely,

Leonard Friedland, MD  
Scientific Affairs and Public Policy  
GlaxoSmithKline Vaccines  
484.620.9540 (mobile)  
[Leonard.R.Friedland@gsk.com](mailto:Leonard.R.Friedland@gsk.com)

---

**From:** Leonard Friedland  
**Sent:** Wednesday, June 05, 2013 4:30 PM  
**To:** 'Destefano, Frank (CDC/OID/NCEZID)'  
**Cc:** Cortese, Margaret (CDC/OID/NCIRD)  
**Subject:** RE: Rotarix VSD Intussusception data

Dear Dr. Destefano,

(b)(4)

(b)(4)

Sincerely,

Leonard Friedland, MD  
Scientific Affairs and Public Policy  
GlaxoSmithKline Vaccines  
484.620.9540 (mobile)  
[Leonard.R.Friedland@gsk.com](mailto:Leonard.R.Friedland@gsk.com)

---

**From:** Destefano, Frank (CDC/OID/NCEZID) [<mailto:fxd1@cdc.gov>]  
**Sent:** Friday, May 03, 2013 10:02 AM  
**To:** Remon Roskoaf Abu-Elyazeed  
**Cc:** Cortese, Margaret (CDC/OID/NCIRD)  
**Subject:** Intussusception data

Dear Dr. Abu-Elyazeed:

Margaret informed me that you were interested in the topic of rotavirus vaccines and intussusception scheduled for an upcoming ACIP meeting. One of the presentations at that session will be findings from our Vaccine Safety Datalink on Rotarix and intussusception. We could provide a confidential preview to you and a limited number of other GSK staff if you are interested.

Frank DeStefano, MD, MPH  
Director  
Immunization Safety Office  
Centers for Disease Control and Prevention  
Atlanta, GA



**From:** Leonard Friedland  
**Sent:** Mon, 15 Jul 2013 11:14:26 +0000  
**To:** Parashar, Umesh (CDC/OID/NCIRD)  
**Cc:** Su-Peing Ng;Seward, Jane (CDC/OID/NCIRD);Cortese, Margaret (CDC/OID/NCIRD);Destefano, Frank (CDC/OID/NCEZID);Dominique Rosillon;Hubert Buyse  
**Subject:** Re: GSK Rotavirus vaccine

Dear Umesh,

We look forward to receiving your comments.

Criteria for a study to be included in the meta-analysis include the availability of a study report or publication. We would appreciate a copy of the VSD study report upon availability.

Best regards, Len

On Jul 12, 2013, at 3:20 PM, "Parashar, Umesh (CDC/OID/NCIRD)" <[uap2@cdc.gov](mailto:uap2@cdc.gov)> wrote:

Dear Len

Appreciate the opportunity to provide feedback.

We will review the materials you shared before and provide feedback, but it will not be possible for us to join formally as coauthors.

The one comment that I already mentioned to you at ACIP was regarding t

(b)(4)

(b)(4)

Best

Umesh

---

**From:** Leonard Friedland [<mailto:Leonard.R.Friedland@gsk.com>]

**Sent:** Thursday, July 11, 2013 7:59 AM

**To:** Parashar, Umesh (CDC/OID/NCIRD)

**Cc:** Su-Peing Ng

**Subject:** GSK Rotavirus vaccine

Dear Umesh,

I am contacting you to ask your availability to speak with me and my GSK colleague Su-Peing Ng to discuss the rotavirus vaccine and intussusception meta-analysis GSK provided to you/CDC on 19 June. We are interested to discuss questions you may have regarding the methodology, additional work to be done, possible interest from you or others at CDC to join as researchers with the meta-analysis.

Please respond with a time to speak later this week or next.

Best regards,

Len

Leonard Friedland, MD

Scientific Affairs and Public Health



North American Vaccine Development  
GlaxoSmithKline Vaccines  
484.620.9540 (mobile)  
[Leonard.R.Friedland@gsk.com](mailto:Leonard.R.Friedland@gsk.com)

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

Dear All:

(b)(6)

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

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

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

New contact information:  
5952 Trippe Creek Drive  
Oxford, MD 21654

443-239-9369 (cell)  
410-770-3686

[mrennels@atlanticbb.net](mailto:mrennels@atlanticbb.net) (after July 8)

**From:** Bailey, Steven R.  
**Sent:** Fri, 10 Feb 2017 14:00:57 +0000  
**To:** Caplanusi Irina;'Corinne.Jouquelet-Royer@sanofipasteur.com';Bachtiar, Novilia (novilia@biofarma.co.id);Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br);Destefano, Frank (CDC/OID/NCEZID);Zuber, Patrick (CDC who.int)  
**Cc:** Karin Holm (karinholm@bluewin.ch);Rago Lembit (ragol@cioms.ch);Heininger, Ulrich;Le\_Roux Susanne  
**Subject:** RE: CIOMS AVSS Final EdBd issues from 15 Dec  
**Attachments:** EXECUTIVE SUMMARY Final 2.docx

Sorry, now with attachment!

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]  
**Sent:** 10 February 2017 13:00  
**To:** Caplanusi Irina; Holm Karin; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); 'Destefano, Frank (CDC/OID/NCEZID)'; Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))  
**Cc:** Karin Holm ([karinholm@bluewin.ch](mailto:karinholm@bluewin.ch)); Rago Lembit ([ragol@cioms.ch](mailto:ragol@cioms.ch)); Heininger, Ulrich; Le\_Roux Susanne  
**Subject:** RE: CIOMS AVSS Final EdBd issues from 15 Dec  
**Importance:** High

Dear Editorial Board:

First, as a quick update. I was recently informed by Lembit that CIOMS should have the guide back from the printers in the next week or two. We will make you aware when it is available.

As part of increasing the awareness of the guide, we had discussed (and reviewed) and Executive Summary that Uli would submit to a number of targeted publications.

I have updated this Executive Summary to better match the final guide. I attached the proposed summary here (in incorporates edits from Uli, Patrick, Irina, and myself). This is largely for your information, but if you do have any edits or suggestions please let me know. I would ask that if you do have an comments/edits, that you forward them all by the end of day on Tuesday of next week, as we want to move this forward in a very timely manner.

Kind regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

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(b)(4)

**From:** Bailey, Steven R.  
**Sent:** Mon, 5 Dec 2016 17:02:23 +0000  
**To:** Bahri Priya; Zuber, Patrick (CDC who.int); Straus, Walter L.; Destefano, Frank (CDC/OID/NCEZID); Holm Karin; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; Rago Lembit; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Caplanusi Irina; Winiecki, Scott (FDA/CBER); MAURE, Christine  
**Subject:** RE: Two Items for your Consideration and Comment

Priya:

(b)(4)

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Bahri Priya [mailto:Priya.Bahri@ema.europa.eu]  
**Sent:** Monday, December 5, 2016 4:58 AM  
**To:** ZUBER, Patrick Louis F.; Bailey, Steven R.; Straus, Walter L.; Destefano, Frank (CDC/OID/NCEZID); Holm Karin; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; Rago Lembit; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Caplanusi Irina; Winiecki, Scott (FDA/CBER); MAURE, Christine  
**Subject:** RE: Two Items for your Consideration and Comment

Dear Steven,

Many thanks, (b)(4)

(b)(4)

(b)(4)

What so the others think?

Thank you again, kind regards Priya

---

**From:** ZUBER, Patrick Louis F. [<mailto:zuberp@who.int>]

**Sent:** 05 December 2016 06:44

**To:** Bailey, Steven R.; Straus, Walter L.; Destefano, Frank (CDC/OID/NCEZID); Holm Karin; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; Rago Lembit; [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); Caplanusi Irina; Winiecki, Scott (FDA/CBER); MAURE, Christine; Bahri Priya

**Subject:** RE: Two Items for your Consideration and Comment

Dear Steven,

Looks good. I have added two comments in support of this version.

Best,

Patrick

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]

**Sent:** 01 December 2016 21:18

**To:** Straus, Walter L.; Destefano, Frank (CDC/OID/NCEZID); Holm Karin; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; ZUBER, Patrick Louis F.; Rago Lembit; [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); Winiecki, Scott (FDA/CBER); MAURE, Christine; [Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)

**Cc:** Bailey, Steven R.

**Subject:** Two Items for your Consideration and Comment

All:

We continue to work on the document to move things forward (Karin has been doing the heavy lifting of incorporating all the additional comments we have been receiving). She continues to work on this.

She and I met this morning to try to resolve as much as we can prior to the editorial board meeting on the 15<sup>th</sup> of December. There were two items that I was asked to resolve after our last meeting that we need input on:

(b)(4)

I have taken a stab at resolving both of these, and my proposals are attached (it is a focused excerpt from the manual: after we resolve we will drop it back in).

(b)(4)

Regards,

Steven.

PS: note: if you feel this is not an area where you have appropriate expertise, and don't want to weigh in, that is fine. But all comments are welcome.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

This e-mail has been scanned for all known viruses by European Medicines Agency.

---



**From:** Leonard Friedland  
**Sent:** Fri, 24 May 2013 18:46:49 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID); Cortese, Margaret (CDC/OID/NCIRD)  
**Subject:** GSK - June ACIP

Dear Frank and Margaret –  
Thank you for arranging the VSD presentation yesterday.  
I expect to contact you next week with questions that will assist us to further understand the data.  
Best regards, Len

Leonard Friedland, MD  
GlaxoSmithKline Vaccines  
610.787.3644 (office)  
484.620.9540 (mobile)  
Leonard.R.Friedland@gsk.com

**From:** Remon Roskoaf Abu-Elyazeed  
**Sent:** Tue, 14 May 2013 01:59:09 +0000  
**To:** Cortese, Margaret (CDC/OID/NCIRD)  
**Cc:** Destefano, Frank (CDC/OID/NCEZID); Leonard Friedland  
**Subject:** June ACIP

Dear Margaret,

I saw the draft ACIP agenda that listed several agenda items under "Rotavirus Vaccines". Will you or any of your colleagues be able to review with GSK the "other" agenda items on VAERS and PRISM. We really appreciate the upcoming preview on the VSD findings on Rotarix and intussusceptions.

Thanks

Sincerely, Remon

**From:** Bailey, Steven R.  
**Sent:** Tue, 15 Nov 2016 03:37:18 +0000  
**To:** Holm Karin;'Corinne.Jouquelet-Royer@sanofipasteur.com';Zuber, Patrick (CDC who.int);Rago Lembit;Paulo.santos@bio.fiocruz.br;novilia@biofarma.co.id;Destefano, Frank (CDC/OID/NCEZID);Irina.Caplanusi@ema.europa.eu;Winiecki, Scott (FDA/CBER);walter\_straus@merck.com;maurec@who.int;Priya.Bahri@ema.europa.eu  
**Subject:** RE: Updated Plan for Document Completion 14 nov

Thanks Karin.

All:

Could I ask all of you to take a careful look at this version, paying special attention to the comments that remain in the document as these will be the focus of our discussion next Tuesday. We will go through each comment and proposed edit and reach consensus on each. If we cannot reach consensus, we will mark these comments for final resolution at the final Editorial Board meeting in December.

If you are able to review and become familiar/form an opinion on these comments ahead of the meeting, we will be able to review much more quickly and efficiently.

Looking forward to review with everyone next week.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Holm Karin [mailto:holmk@cioms.ch]  
**Sent:** Monday, November 14, 2016 5:40 PM  
**To:** Bailey, Steven R.; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; zuberp@who.int; Rago Lembit; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; fxd1@cdc.gov; Irina.Caplanusi@ema.europa.eu; Scott.Winiecki@fda.hhs.gov; walter\_straus@merck.com; maurec@who.int; Priya.Bahri@ema.europa.eu; Holm Karin  
**Cc:** Holm Karin  
**Subject:** Updated Plan for Document Completion 14 nov

Dear All,  
Attached please find the current version 14 Nov to be reviewed by the EdBd Plus which includes a few issues for the EdBoard to decide how to handle on the TC on Nov.22 . Hopefully the Table 5 EVI in Appendix I is more understandable and usable now (I edited it carefully based on input from WHO).  
Best regards,  
Karin

---

**Karin R. Holm**

Technical Collaboration Coordinator, WG on Vaccine Safety

Publications Coordinator, WG X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

Associate partner of UNESCO and in official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland

Ofc Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)

Email: [holmkr@cioms.ch](mailto:holmkr@cioms.ch)

---

-

**From:** Bailey, Steven R.  
**Sent:** Wed, 9 Nov 2016 14:11:18 +0000  
**To:** 'Corinne.Jouquelet-Royer@sanofipasteur.com'; Zuber, Patrick (CDC who.int); ragol@cioms.ch; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Destefano, Frank (CDC/OID/NCEZID); Irina.Caplanusi@ema.europa.eu; holmk@cioms.ch; holmk@cioms.ch; novilia@biofarma.co.id; ragol@cioms.ch; Zuber, Patrick (CDC who.int); Paulo.santos@bio.fiocruz.br; Destefano, Frank (CDC/OID/NCEZID); Irina.Caplanusi@ema.europa.eu; Winiecki, Scott (FDA/CBER); walter\_straus@merck.com; maurec@who.int; Corinne.Jouquelet-Royer@sanofipasteur.com; Priya.Bahri@ema.europa.eu; Rago Lembit (ragol@cioms.ch)  
**Cc:** Bailey, Steven R.  
**Subject:** Updated Plan for Document Completion

All:

We just had a meeting of a small group (select editorial board members and other key reviewers). The original intent of this meeting was to perform a review of the updated document ahead of the editorial board meeting on the 22<sup>nd</sup> of November (optimistically titled "final meeting of the editorial board").

Because we did not quite have the document ready for review (which contains key inputs from LMIC stakeholders and Christine/Karin), we made a rapid change in plans. I will outline this below, and will send more details when I have a bit more time:

- 1) Karin will work on the document today, and incorporate inputs from Christine and herself into one document.
- 2) Karin will forward the document to Patrick and myself, who will further edit this version. We are committed to return this to her by next Monday.
- 3) Karin will then take this version, and clean the document up and ready it for team review on the 22<sup>nd</sup>. She will aim to send this version out to the team by next Thursday the 17<sup>th</sup>.
- 4) **Instead of the "final EB meeting", the meeting on the 22<sup>nd</sup> (8-10 EST) will be used to clean up the document, and accept as many comments as we can.** I will forward the invite to that meeting to the editorial plus members. During that meeting we will review the document, accept changes, and highlight areas that need further work/input from LMIC regulatory stakeholders.
- 5) The document will be sent on November 23<sup>rd</sup> to identified LMIC Regulatory stakeholder who will be asked to return comments by December 7<sup>th</sup>.
- 6) Karin will collate their comments into the document, and will likely circulate for review/preread amongst the editorial board (I will review with her first).
- 7) We will look for a date to hold a final "Final Editorial Board Meeting" the week of December 11<sup>th</sup>. (I will send a separate e-mail to EB to schedule later today.
- 8) If all goes as planned above, this will delay our publication by 3-4 weeks. Rather than publishing before Christmas, we will be looking at mid-January.

If anyone who was on this morning's call thinks I got something wrong, or I left something out, please send a note. And if anyone has any questions or concerns, please reach out to (copying all). Hopefully we will soon consider this our revised plan, and if we execute, we will be on track for January.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670



**From:** Straus, Walter L.  
**Sent:** Thu, 1 Dec 2016 08:33:17 -0500  
**To:** Destefano, Frank (CDC/OID/NCEZID); Holm Karin; 'Bailey, Steven R.'; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; Zuber, Patrick (CDC who.int); Rago Lembit; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Irina.Caplanusi@ema.europa.eu; Winiecki, Scott (FDA/CBER); maurec@who.int; Priya.Bahri@ema.europa.eu  
**Subject:** RE: CIOMS AVSS Final comments pp.47-65  
**Attachments:** CIOMS guide AVSS\_22\_Nov fxd-ws.docx

Karin,

I've added a few final suggested tweaks to the outstanding section, as well as to the ethics section).  
Best,

*Walter*

---

**Walter L. Straus, MD, MPH, FCPP, FACP** Associate Vice President and Therapeutic Area Head, Clinical Safety and Risk Management 2 (Infectious Diseases and Vaccines), Merck Research Laboratories, Merck & Co., Inc., 351 North Sumneytown Pike, North Wales, PA 19454 / Tel: 267-305-7143 / Fax: 215-616-1095  
Assistant: Jane Detweiler jane\_detweiler@merck.com Tel: 267-305-7027

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**From:** Destefano, Frank (CDC/OID/NCEZID) [mailto:fxd1@cdc.gov]  
**Sent:** Wednesday, November 23, 2016 3:50 PM  
**To:** Holm Karin; 'Bailey, Steven R.'; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; Zuber, Patrick (CDC who.int); Rago Lembit; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Irina.Caplanusi@ema.europa.eu; Winiecki, Scott (FDA/CBER); Straus, Walter L.; maurec@who.int; Priya.Bahri@ema.europa.eu  
**Subject:** RE: CIOMS AVSS Final comments pp.47-65

Attached are my responses to sections that I wrote.  
Thanks,  
Frank

Frank DeStefano, MD, MPH

---

**From:** Holm Karin [mailto:holm@cioms.ch]  
**Sent:** Tuesday, November 22, 2016 12:21 PM  
**To:** 'Bailey, Steven R.' <Steven.R.Bailey@pfizer.com>; 'Corinne.Jouquelet-Royer@sanofipasteur.com' <Corinne.Jouquelet-Royer@sanofipasteur.com>; Zuber, Patrick (CDC who.int) <zuber@who.int>; Rago Lembit <ragol@cioms.ch>; Paulo.santos@bio.fiocruz.br; novilia@biofarma.co.id; Destefano, Frank (CDC/OID/NCEZID) <fxd1@cdc.gov>; Irina.Caplanusi@ema.europa.eu; Winiecki, Scott (FDA/CBER) <Scott.Winiecki@fda.hhs.gov>; walter\_straus@merck.com; maurec@who.int; Priya.Bahri@ema.europa.eu; Holm Karin

<[holmk@cioms.ch](mailto:holmk@cioms.ch)>

**Subject:** CIOMS AVSS Final comments pp.47-65

Dear Ed Board Plus,

Thank you so much for contributing today.

Assignments for Steven and Karin to tweak and Patrick (mening case in section 1.5)

Rest of Group: Please look at only the last 5-6 clusters of comments that we didn't get to between **pages 47-65**. Please get us your comments by **Monday, 28 Nov**.

Best regards,

Karin

**Karin R. Holm**

Technical Collaboration Coordinator, Working Group on Vaccine Safety

Publications Coordinator, CIOMS X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

c/o WCC, P.O. Box 2100 CH-1211 Geneva 2, Switzerland

Office Phone: +41 22 791 6497 [www.cioms.ch](http://www.cioms.ch)

Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

*(CIOMS is an Associate Partner of UNESCO and in Official Relations with WHO.)*

---

**From:** Bailey, Steven R. [<mailto:Steven.R.Bailey@pfizer.com>]

**Sent:** 21 November 2016 14:40

**To:** 'Corinne.Jouquelet-Royer@sanofipasteur.com'; [zuberp@who.int](mailto:zuberp@who.int); Rago Lembit;

[Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); [novilia@biofarma.co.id](mailto:novilia@biofarma.co.id); [fxd1@cdc.gov](mailto:fxd1@cdc.gov);

[Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); Holm Karin; [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov);

[walter\\_straus@merck.com](mailto:walter_straus@merck.com); [maurec@who.int](mailto:maurec@who.int); [Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)

**Subject:** Tomorrow

All:

(b)(6)

Both the telecon and webex will be available before I join (the webex will default to the first to join, but can be passed around). Given how much we have to work on, I would suggest you all start working before I join. If someone can take the lead, it should be enough to just move from comment to comment in the document, as this is what need consensus by the team. It should be fairly straightforward, as most comments have corresponding comments/opinions from Patrick, Karin, Novi, or myself. If the group is in agreement, just make the necessary changes, delete the comments, and move on. If the group feel the editorial board needs to formally consider further, mark this section as such.

Please use the attached version (with Novi's comments included).



Regards, and thanks,

Steven.

PS: if there is a problem with the webex, you can call my cell: (b)(6) although I will try to call in at 8:00 from the car).

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

---

**From:** Novilia [<mailto:novilia@biofarma.co.id>]  
**Sent:** Monday, November 21, 2016 3:47 AM  
**To:** Holm Karin  
**Cc:** Bailey, Steven R.  
**Subject:** RE: Updated Plan for Document Completion 14 nov

Dear Karin and Steven,

I plan to join the TC tomorrow night. I will be in Jakarta using the hotel internet Access tomorrow, in case of I can't connect tomorrow, here with my comments.

Best regards,  
Novi

---

**From:** Holm Karin [<mailto:holmkarin@cioms.ch>]  
**Sent:** Selasa, November 15, 2016 5:40 AM  
**To:** Bailey, Steven R.; 'Corinne.Jouquelet-Royer@sanofipasteur.com'; [zuberp@who.int](mailto:zuberp@who.int); Rago Lembit; [Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br); Novilia; [fxd1@cdc.gov](mailto:fxd1@cdc.gov); [Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu); [Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov); [walter\\_straus@merck.com](mailto:walter_straus@merck.com); [maurec@who.int](mailto:maurec@who.int); [Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu); Holm Karin  
**Cc:** Holm Karin  
**Subject:** Updated Plan for Document Completion 14 nov

Dear All,  
Attached please find the current version 14 Nov to be reviewed by the EdBd Plus which includes a few issues for the EdBoard to decide how to handle on the TC on Nov.22 . Hopefully the Table 5 EVI in Appendix I is more understandable and usable now (I edited it carefully based on input from WHO).  
Best regards,  
Karin

---

**Karin R. Holm**

Technical Collaboration Coordinator, WG on Vaccine Safety

Publications Coordinator, WG X Meta-Analysis

Council for International Organizations of Medical Sciences (CIOMS)

Associate partner of UNESCO and in official relations with WHO  
c/o WCC, P.O. Box 2100, CH-1211 Geneva 2, Switzerland

Ofc Phone: +41 22 791 6497 Website: [www.cioms.ch](http://www.cioms.ch)

Email: [holmk@cioms.ch](mailto:holmk@cioms.ch)

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**From:** Bailey, Steven R.  
**Sent:** Thu, 1 Dec 2016 20:18:11 +0000  
**To:** Straus, Walter L.;Destefano, Frank (CDC/OID/NCEZID);Holm Karin;'Corinne.Jouquelet-Royer@sanofipasteur.com';Zuber, Patrick (CDC who.int);Rago Lembit;Paulo.santos@bio.fiocruz.br;novilia@biofarma.co.id;Irina.Caplanusi@ema.europa.eu;Winiecki, Scott (FDA/CBER);maurec@who.int;Priya.Bahri@ema.europa.eu  
**Cc:** Bailey, Steven R.  
**Subject:** Two Items for your Consideration and Comment  
**Attachments:** CIOMS guide AVSS\_1\_Dec srb Table 2 Only.docx

All:

We continue to work on the document to move things forward (Karin has been doing the heavy lifting of incorporating all the additional comments we have been receiving). She continues to work on this.

She and I met this morning to try to resolve as much as we can prior to the editorial board meeting on the 15<sup>th</sup> of December. There were two items that I was asked to resolve after our last meeting that we need input on:

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I have taken a stab at resolving both of these, and my proposals are attached (it is a focused excerpt from the manual: after we resolve we will drop it back in).

(b)(4)

Regards,

Steven.

PS: note: if you feel this is not an area where you have appropriate expertise, and don't want to weigh in, that is fine. But all comments are welcome.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

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(b)(4)

**From:** Bailey, Steven R.  
**Sent:** Fri, 29 Apr 2016 18:35:00 +0000  
**To:** 'Straus, Walter (walter\_straus@merck.com)'; Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Heininger, Ulrich; Holm Karin; Bachtiar, Novilia (novilia@biofarma.co.id); Bahri, Priya (Priya.Bahri@ema.europa.eu); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Darko, Mim (b)(6); Destefano, Frank (CDC/OID/NCEZID); Dodoo, Alex (b)(6); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); Maure, Christine (maurec@who.int); Winiecki, Scott (FDA/CBER); Zuber, Patrick (CDC who.int)  
**Subject:** RE: CIOMS Meeting

All:

PLEASE READ and raise any issues/questions

First, thanks to everyone who was able to call in this morning. We had a small group, but it was productive in helping determine next steps.

As discussed by e-mail, the majority have landed on the "hybrid" approach to sequential review: for the next 3 week we will have individual reviewers who will sequentially review, with a team review of the updates every Friday. This will be followed by a final review by this entire group from May 20<sup>th</sup> to May 25<sup>th</sup> (with some room for the 26<sup>th</sup>), with a critical team meeting on the 27<sup>th</sup> to finalize a draft going to the external SMEs.

Unfortunately, the document was not quite ready to begin the review process today. Instead, Karin will work through a few remaining items and we will begin our sequential review on Monday/Tuesday of next week. Please provide Karin with anything she needs to ensure we have a single document to begin this process on time.

As far as sequential review, here is the schedule:

Date	Days	Who
Apr 29- May 2	Fri-Mon	Karin Finalizing Document
May 2- May 6	Mon-Fri	Scott Winiecki
May 6- May 10	Fri-Tues	Frank
May 10- May 13	Tues-Fri	Irina Caplanusi
May 13- May 16	Fri-Mon	Patrick Zuber
May 16- May 20	Mon-Fri	Steven Bailey
May 20-May 25	Fri-Wed	All Remaining Reviewers

Some notes on this schedule

1. Thanks to all who volunteered to perform sequential review, and Scott for offering to go first
2. Although we have filled all spot, we would still **very much like to get a reviewer** from a resource limited country to be part of this important process. If possible, we would like them to take



Frank's slot May 6<sup>th</sup>-May 9. I have not heard from a number of you, but if **Alex, Novilia or Paulo** would be willing to be part of the individual sequential review, we believe it would be very helpful to have their insight in that slot. Please let us know if you can volunteer.

A few other critical points:

The Intro and the Intro to the EVI-C: currently we are awaiting inputs from Walter, and then some review of that by Patrick and others. Hopefully Karin and I can touch base with **Walter** on Monday, and we will see where that stands. For now sequential review will begin without these sections, and we will add them in as soon as they are ready.

Meetings: We realize everyone is busy, but your participation is essential to moving this forward. Starting next week, the Friday meetings will be decision making meeting: we will take the results of the weekly sequential reviews, and accept or reject any edits or comments. We will then need to move on in an aligned fashion. So it is critical we have as many of us as possible on the Friday calls.

**Especially important will be the May 27<sup>th</sup> meeting:** if you can only attend one meeting, please prioritize this one: we will have just completed review by all remaining members, and it will be important that we have all editors/reviewers available so we can finish the document up during the meeting, and get this to the outside SMEs who will be reviewing. Their time is very limited, and we have to get it to them quickly, and we will be coordinating comments from about half this group. Please block this time if you can.

As far as that final review week (May 20<sup>th</sup>-May 25/26): This will be the primary review by 10 of the 15 people included on this e-mail. If you are not a sequential reviewer, please mark some time to review during that time period. It will be important to complete your review by the 25<sup>th</sup> as I will be receiving up to 10 different versions of the document and will need to consolidate prior to the 27<sup>th</sup>. I will need May 26<sup>th</sup> to do this.

Finally, some general rules of the road for your review:

1. Version control is going to be difficult. Please append your name and date to any version you review so we can track the differing versions. Every Friday we will update the version after the team review
2. If it is not your turn to review (sequential reviewer or during the team review), please hold your comments/edits until it is your turn. We will not be able to track edits/comments if they are coming in separate versions or e-mails. If you want to review ahead of time, feel free to take notes in whatever version you have, but you will need to transfer them to the official version when your turn comes.
3. When editing, please use the word functions for track changes and comments. Make sure your initials or name are set in your version of word so it will track who made the comments or edits.
4. Please plan on attending the Friday meeting after your review: we will need the reviewer there to explain their comments and edits.
5. Please provide suggestion/text for any comments you have, or note they are simply for discussion. At this stage, we cannot simply have a comment saying "it would be good to add a section about XXXX here". If you want to add something, please author it so we can make a decision about inclusion at the Friday meeting. If you want to wait to see if everyone agrees,



mark it with a comment for discussion, but be prepared to provide any additional text suggested.

I hope all this makes sense. Reach out if questions. If we all commit to doing our part, we will get this done in our tight timelines.

Unfortunately I cannot attend next Friday, but Karin has kindly offered to lead the group. We look forward to actually having the who documents, with the first completed review, at that point next week (thanks Karin and Scott!).

Thanks all. Have a great weekend.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** Bailey, Steven R.

**Sent:** Friday, April 22, 2016 2:43 PM

**To:** 'Straus, Walter (walter\_straus@merck.com)'; Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Heininger, Ulrich; Holm Karin; Bachtiar, Novilia (novilia@biofarma.co.id); Bahri, Priya (Priya.Bahri@ema.europa.eu); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Darko, Mimi (b)(6); DeStefano, Frank (fxd1@cdc.gov); Dodoo, Alex (b)(6); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); Maure, Christine (maurec@who.int); Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov); Zuber, Patrick (zuberp@who.int)

**Cc:** Bailey, Steven R.

**Subject:** RE: CIOMS Meeting

**Importance:** High

All: This is a long e-mail, but please review carefully, and respond as requested so we can be ready by next Friday to begin the final Editorial Review.

This is a follow up message from our meeting this morning (the first of our weekly Friday calls for this group). Thanks to all who were able to attend,. We had a very productive meeting, and set forth a plan for reaching our goal of "Print Ready by July 1"!

We made a few logistical decisions which will support the continued work and review by the Editorial Board (plus) over the next few months. High level we agreed on the following approach:

1. Between now and next Wednesday, we will endeavor to complete the few remaining open pieces, which will allow Karin to put together a complete draft (all TGs) for next Friday, at which point we will start...

2. Sequential Review of the Big Document by the Editorial Board, aiming to complete this review by May 27<sup>th</sup>. This “near final” version will then go to...
3. The entire CIOMS group plus ~5 Experts from outside the group (being arranged now). They will have from May 27<sup>th</sup> to June 14<sup>th</sup> for this review. And we will provide instructions on the level to which they should review and how much can be changed at that point. Their comments will then go to
4. The editorial board who will have a very quick turnaround time (June 15<sup>th</sup> to June 22<sup>nd</sup>) to consider their comments and finalize the document before it goes to an editorial consultant and then Print Ready.

Now, some organization details for these steps. Please read carefully, and let us know if you object (if you were not on line). And please responds to some important questions for the group to weigh in on

**For One (finalize remaining pieces before EB review):** Karin will be cracking the whip (nicely, as she does). All key folks for doing this were on the line I think this morning. We would appreciate everyone’s help in providing these last bits in pieces in a timely manner (by next Wednesday)

**For Two (Sequential Review):** This may be the most complex piece (for scheduling at least). So let me propose some options, and please weigh in on preference. We will go with the majority opinion.

We will not be able to begin the sequential review until next Friday when step 1 above is complete. We will then have 4 full weeks to complete. (28 days). Not that each week will be punctuated with a Friday meeting of the group

My initial proposal was that we set a hard schedule for sequential review: each week we would have 2 slots (F-M and Tu-F), and everyone would choose a 3 or 4 day slot that they could commit to, and we would hold everyone firmly to these slots, reviewing two updates at the Friday meeting to keep the edits updated and not have too much to review at the end.

The problem is that I did not realized how many of us were on this group at this point (15), and that we had only 4 weeks (I thought it was 5). So, we would only have 8 slots for 15 people.

Which leaves us with a few options (if we want sequential review)

- a. Everyone has a chance at a sequential review: We would have to set up a schedule with 2 day slots. People would have to be very focused, and logistically prone to difficulties/weekends/loss of version control
- b. We stick with the proposal of just 2 reviews per week (already tight), but limit to just 8 reviewers (we can see who prefers to review and who not to review)
- c. A hybrid: We obtain 6 volunteer to perform full sequential review, and do this for the first 3 weeks (3 to 4 days each), and update document each Friday. Then, the last week, we take the document (which will have been reviewed carefully by 6 of us), and send out for all the remaining folks (about 8) to have 5 days to provide any last suggested changes. If done by the 25<sup>th</sup>, I could then merge all of the different versions from this group review. Then on the 27<sup>th</sup> we can all meet and accept/reject these last group changes, and send on for the expert review/fully CIOMS review.

My preference is option C: I think this will work because by the time we do 6 individual reviews, we will not likely have extensive comments when it goes to the other 8 or 9 folks.



**PLEASE** let me (and the group) know your preference for which of these options. And please do so by MONDAY end of day (the 25<sup>th</sup>). I will then put together a schedule for the review before next Friday. In addition to your overall approach preference, please let me know:

- i. Do you prefer to be one of the sequential reviewers, a group reviewer, or not review at all
- ii. If one of the sequential reviewer, which review slots would work for you (that is, date chunks that would work for you to COMMIT to get your sequential review complete (handoff times on common days will be negotiated. Updates must be complete by the time of our Friday meeting)
  - a. APR 29- May 2
  - b. May 2- May 6
  - c. May 6- May 9
  - d. May 9- May13
  - e. May 13- May 16
  - f. May 16- May 20
  - g. May 20- May 23 (this slot would be group review under option C)
  - h. May 23- May 27 (this slot would be group review under option C)

Sorry for the complexity of this planning, but once we have this set it will allow us to move this forward, and track that we are staying on point.

**For Three (the final push):** We all agreed that we need to dedicate a lot of dedicated time for the EB to review all the final comments from experts and larger group. We also agreed that travel to one site in EU or US was not supportable. Therefore we will look at options for long, dedicated telecons/Videocons, perhaps from a site on each continent (plus phone). We will work out the details of this later, but for now **please lock your calendars**, as much as you can, for June 15, 16 and 17. Esp. important will be the mornings for US folks, and afternoons for EU folks, when we can all work together. If you can get this time on your calendar now before it fills up, it will allow us to get all we need to that last working week. We will work on logistics at the Friday meetings, and free up calendars as possible. (note this will give us a few days (the 20<sup>th</sup>/21<sup>st</sup>) leeway to take care of anything else)

I thank any of you who have made it this far through the e-mail. Sorry for complexity, but we have a lot to do, a large group, and very limited time. If we stay organized, we will get it all done, and avoid duplication of work and/or loss of version control. And from experience, if we don't block calendars, something will come up and take precedence. So:

- a. Work with Karin to get the full document read to go by next Wednesday
- b. Please let me know your preferences on sequential review, and please volunteer to be a reviewer, and when you can do it if you can
- c. Please block your calendar for June 15-17

Many thanks, and have a great weekend.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
Vice President, Worldwide Safety and Regulatory  
SSRM RU/Vaccines Group Head  
Pfizer  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

-----Original Appointment-----

**From:**

**Sent:** Wednesday, April 13, 2016 9:38 AM

**To:** Bailey, Steven R.; 'Straus, Walter ([walter\\_straus@merck.com](mailto:walter_straus@merck.com))'; Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Heininger, Ulrich; Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi ([\(b\)\(6\)](#)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ([\(b\)\(6\)](#)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Subject:** CIOMS Meeting

**When:** Friday, April 22, 2016 9:00 AM-11:00 AM (UTC-05:00) Eastern Time (US & Canada).

**Where:** Webex

**\*Steven Bailey to host\***

*Setting these meetings to recur weekly beginning April 22<sup>nd</sup> through mid-July @ 9-11 AM (EDT).*

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Meeting Information

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<https://collaborate.webex.com/collaborate/j.php?MTID=m4e965733b6fe6082a928df698699321d>

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(b)(6)

Call-in toll-free number (US/Canada)

Call-in toll number (US/Canada)

Access code:

(b)(6)

Global call-in numbers:

<https://collaborate.webex.com/collaborate/globalcallin.php?serviceType=MC&ED=431206297&tollFree=1>

Toll-free dialing restrictions:

[http://www.webex.com/pdf/tollfree\\_restrictions.pdf](http://www.webex.com/pdf/tollfree_restrictions.pdf)

WebEx Meeting and Support Details

Meeting number: (b)(6)

Meeting password: (b)(6)

Host key (b)(6)

IMPORTANT NOTICE: Please note that this WebEx service allows audio and other information sent during the session to be recorded, which may be discoverable in a legal matter. You should inform all meeting attendees prior to recording if you intend to record the meeting.



**From:** Bailey, Steven R.  
**Sent:** Mon, 25 Apr 2016 12:22:37 +0000  
**To:** Zuber, Patrick (CDC who.int); 'Straus, Walter (walter\_straus@merck.com)'; Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Heininger, Ulrich; Holm Karin; Bachtiar, Novilia (novilia@biofarma.co.id); Bahri, Priya (Priya.Bahri@ema.europa.eu); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Darko, Mimi (b)(6); Destefano, Frank (CDC/OID/NCEZID); Dodoo, Alex (b)(6); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); MAURE, Christine; Winiecki, Scott (FDA/CBER)  
**Subject:** RE: CIOMS Meeting

Thanks Patrick. I will await further responses, but will begin to put a schedule together based on your and Scott's feedback.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

---

**From:** ZUBER, Patrick Louis F. [mailto:zuberp@who.int]  
**Sent:** Monday, April 25, 2016 4:14 AM  
**To:** Bailey, Steven R.; 'Straus, Walter (walter\_straus@merck.com)'; Santos, Paulo (alt) (Paulo.santos@bio.fiocruz.br); Heininger, Ulrich; Holm Karin; Bachtiar, Novilia (novilia@biofarma.co.id); Bahri, Priya (Priya.Bahri@ema.europa.eu); Caplanusi, Irina (alt) (Irina.Caplanusi@ema.europa.eu); Darko, Mimi (b)(6); DeStefano, Frank (fxd1@cdc.gov); Dodoo, Alex (b)(6); Jouquelet-Royer, Corinne (Corinne.Jouquelet-Royer@sanofipasteur.com); MAURE, Christine; Winiecki, Scott (alt) (Scott.Winiecki@fda.hhs.gov)  
**Subject:** RE: CIOMS Meeting

Dear Steven and colleagues,

I would favour the hybrid option and would volunteer to be one of the 6 reviewers. This week, I will complete Pryia's assignment for the large communication piece from TG3.

Christine remains the TG2 member for any outstanding issue this week.

With best wishes,

Patrick

---

**From:** Bailey, Steven R. [mailto:Steven.R.Bailey@pfizer.com]  
**Sent:** Friday, April 22, 2016 8:43 PM

**To:** 'Straus, Walter ([walter\\_straus@merck.com](mailto:walter_straus@merck.com))'; Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Heininger, Ulrich; Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi (b)(6); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex (b)(6); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); MAURE, Christine; Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); ZUBER, Patrick Louis F.

**Cc:** Bailey, Steven R.

**Subject:** RE: CIOMS Meeting

**Importance:** High

All: This is a long e-mail, but please review carefully, and respond as requested so we can be ready by next Friday to begin the final Editorial Review.

This is a follow up message from our meeting this morning (the first of our weekly Friday calls for this group). Thanks to all who were able to attend,. We had a very productive meeting, and set forth a plan for reaching our goal of "Print Ready by July 1"!

We made a few logistical decisions which will support the continued work and review by the Editorial Board (plus) over the next few months. High level we agreed on the following approach:

1. Between now and next Wednesday, we will endeavor to complete the few remaining open pieces, which will allow Karin to put together a complete draft (all TGs) for next Friday, at which point we will start...
2. Sequential Review of the Big Document by the Editorial Board, aiming to complete this review by May 27<sup>th</sup>. This "near final" version will then go to...
3. The entire CIOMS group plus ~5 Experts from outside the group (being arranged now). They will have from May 27<sup>th</sup> to June 14<sup>th</sup> for this review. And we will provide instructions on the level to which they should review and how much can be changed at that point. Their comments will then go to
4. The editorial board who will have a very quick turnaround time (June 15<sup>th</sup> to June 22<sup>nd</sup>) to consider their comments and finalize the document before it goes to an editorial consultant and then Print Ready.

Now, some organization details for these steps. Please read carefully, and let us know if you object (if you were not on line). And please responds to some important questions for the group to weigh in on

**For One (finalize remaining pieces before EB review):** Karin will be cracking the whip (nicely, as she does). All key folks for doing this were on the line I think this morning. We would appreciate everyone's help in providing these last bits in pieces in a timely manner (by next Wednesday)

**For Two (Sequential Review):** This may be the most complex piece (for scheduling at least). So let me propose some options, and please weigh in on preference. We will go with the majority opinion. We will not be able to begin the sequential review until next Friday when step 1 above is complete. We will then have 4 full weeks to complete. (28 days). Not that each week will be punctuated with a Friday meeting of the group

My initial proposal was that we set a hard schedule for sequential review: each week we would have 2 slots (F-M and Tu-F), and everyone would choose a 3 or 4 day slot that they could commit to, and we would hold everyone firmly to these slots, reviewing two updates at the Friday meeting to keep the edits updated and not have too much to review at the end.



The problem is that I did not realized how many of us were on this group at this point (15), and that we had only 4 weeks (I thought it was 5). So, we would only have 8 slots for 15 people.

Which leaves us with a few options (if we want sequential review)

- a. Everyone has a chance at a sequential review: We would have to set up a schedule with 2 day slots. People would have to be very focused, and logistically prone to difficulties/weekends/loss of version control
- b. We stick with the proposal of just 2 reviews per week (already tight), but limit to just 8 reviewers (we can see who prefers to review and who not to review)
- c. A hybrid: We obtain 6 volunteer to perform full sequential review, and do this for the first 3 weeks (3 to 4 days each), and update document each Friday. Then, the last week, we take the document (which will have been reviewed carefully by 6 of us), and send out for all the remaining folks (about 8) to have 5 days to provide any last suggested changes. If done by the 25<sup>th</sup>, I could then merge all of the different versions from this group review. Then on the 27<sup>th</sup> we can all meet and accept/reject these last group changes, and send on for the expert review/fully CIOMS review.

My preference is option C: I think this will work because by the time we do 6 individual reviews, we will not likely have extensive comments when it goes to the other 8 or 9 folks.

**PLEASE** let me (and the group) know your preference for which of these options. And please do so by MONDAY end of day (the 25<sup>th</sup>). I will then put together a schedule for the review before next Friday. In addition to your overall approach preference, please let me know:

- i. Do you prefer to be one of the sequential reviewers, a group reviewer, or not review at all
  - ii. If one of the sequential reviewer, which review slots would work for you (that is, date chunks that would work for you to COMMIT to get your sequential review complete (handoff times on common days will be negotiated. Updates must be complete by the time of our Friday meeting)
- a. APR 29- May 2
  - b. May 2- May 6
  - c. May 6- May 9
  - d. May 9- May13
  - e. May 13- May 16
  - f. May 16- May 20
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- c. Please block your calendar for June 15-17

Many thanks, and have a great weekend.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
[Steven.R.Bailey@Pfizer.com](mailto:Steven.R.Bailey@Pfizer.com)  
484 865 3670

-----Original Appointment-----

**From:**

**Sent:** Wednesday, April 13, 2016 9:38 AM

**To:** Bailey, Steven R.; 'Straus, Walter ([walter\\_straus@merck.com](mailto:walter_straus@merck.com))'; Santos, Paulo (alt) ([Paulo.santos@bio.fiocruz.br](mailto:Paulo.santos@bio.fiocruz.br)); Heininger, Ulrich; Holm Karin; Bachtiar, Novilia ([novilia@biofarma.co.id](mailto:novilia@biofarma.co.id)); Bahri, Priya ([Priya.Bahri@ema.europa.eu](mailto:Priya.Bahri@ema.europa.eu)); Caplanusi, Irina (alt) ([Irina.Caplanusi@ema.europa.eu](mailto:Irina.Caplanusi@ema.europa.eu)); Darko, Mimi ((b)(6)); DeStefano, Frank ([fxd1@cdc.gov](mailto:fxd1@cdc.gov)); Dodoo, Alex ((b)(6)); Jouquelet-Royer, Corinne ([Corinne.Jouquelet-Royer@sanofipasteur.com](mailto:Corinne.Jouquelet-Royer@sanofipasteur.com)); Maure, Christine ([maurec@who.int](mailto:maurec@who.int)); Winiecki, Scott (alt) ([Scott.Winiecki@fda.hhs.gov](mailto:Scott.Winiecki@fda.hhs.gov)); Zuber, Patrick ([zuberp@who.int](mailto:zuberp@who.int))

**Subject:** CIOMS Meeting

**When:** Friday, April 22, 2016 9:00 AM-11:00 AM (UTC-05:00) Eastern Time (US & Canada).

**Where:** Webex

**\*Steven Bailey to host\***

*Setting these meetings to recur weekly beginning April 22<sup>nd</sup> through mid-July @ 9-11 AM (EDT).*

-- Do not delete or change any of the following text. --

## Meeting Information

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Access code: (b)(6)

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(b)(6)

Toll-free dialing restrictions:

[http://www.webex.com/pdf/tollfree\\_restrictions.pdf](http://www.webex.com/pdf/tollfree_restrictions.pdf)

WebEx Meeting and Support Details

Meeting number:

(b)(6)

Meeting password

Host key: 668167

(b)(6)

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**From:** Bailey, Steven R.  
**Sent:** Wed, 4 May 2016 14:23:41 +0000  
**To:** Destefano, Frank (CDC/OID/NCEZID)  
**Cc:** Holm Karin  
**Subject:** Sequential Review

Frank:

Good news (I think): Alex DoDoo has agreed to be a sequential reviewer, and will take your slot from this Friday to next Monday. So you will not need to do a sequential review this weekend.

Regards,

Steven.

Steven R. Bailey, MD MPH MBA  
*Vice President, Worldwide Safety and Regulatory*  
*SSRM RU/Vaccines Group Head*  
*Pfizer*  
Steven.R.Bailey@Pfizer.com  
484 865 3670

**From:** Straus, Walter L.  
**Sent:** Wed, 18 May 2016 22:37:56 -0400  
**To:** Steven Bailey; holmk@cioms.ch  
**Cc:** Zuber, Patrick (CDC who.int); Destefano, Frank (CDC/OID/NCEZID)  
**Subject:** Revised CIOMS manual  
**Attachments:** CIOMS Manual on Vaccine Active Safety Surveillance.docx

Dear Steven and Karin,

Attached, as discussed, is the revised document. I focused on the introduction, and made a few changes to the forward (that I had previously drafted).

In these sections, I made revisions, then accepted the changes (and deleted the comments). My revisions are marked in read.

Best,

Walter

**Walter L. Straus, MD, MPH, FCPP, FACP** | Associate Vice President and Therapeutic Area Head | Clinical Safety and Risk Management / Infectious Diseases and Vaccines | Merck Research Laboratories | Merck & Co., 351 North Sumneytown Pike, North Wales, PA 19454  
T: 267-305-7143 | F: 215-616-1095 | Assistant: Jane Detweiler [jane\\_detweiler@merck.com](mailto:jane_detweiler@merck.com) T: 267-305-7027

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