

FLU THIMEROSAL

Bernier, Roger

From: Strikas, Ray
Sent: Wednesday, September 29, 1999 5:12 PM
To: Strikas, Ray; Fukuda, Keiji; Bridges, Carolyn; Sinks, Tom; Kilbourne, Edwin M., M.D.; Falk, Henry; De Rosa, Christopher (Chris); Mawle, Alison; O'Connor, Dawn E.; Dowell, Scott; Mast, Eric; Margolis, Harold
Cc: Bernier, Roger; Livengood, John; Wharton, Melinda; Cox, Nancy; Breiman, Robert F; Myers, Martin G.
Subject: RE: Please attend conference call to discuss CDC positions on thimerosal containing vaccines

Point of clarification, after some questions arose:

The call will focus on item 4, in an effort to develop interim guidance for CDC staff that can be used to handle public inquiries (but not for publication), as well as see if developing more detailed information later is desirable. This discussion will help us develop suggestions for the ACIP as it ponders the need and content for any possible publication on this issue. We will rely on the ACIP to recommend the final approach to any publication (i.e., Notice to Readers in MMWR), which would be issued under their name. We can also decide if and how, paraphrasing Dixie Snider, a detailed scientific "deliberative process [will occur at CDC] and [how to] report the outcome in an appropriate medium."

In discussing the influenza matter, general themes and outstanding issues on thimerosal may come up, which will help us in presenting items 1-3 to ACIP. If time permits next week, we may discuss these in turn briefly.

Thank you.

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

From: Strikas, Ray
Sent: Wednesday, September 29, 1999 3:29 PM
To: Fukuda, Keiji; Bridges, Carolyn; Sinks, Tom; Kilbourne, Edwin M., M.D.; Falk, Henry; De Rosa, Christopher (Chris); Mawle, Alison; O'Connor, Dawn E.; Dowell, Scott; Mast, Eric; Margolis, Harold
Cc: Bernier, Roger; Livengood, John; Wharton, Melinda; Cox, Nancy; Strikas, Ray; Breiman, Robert F; Myers, Martin G.
Subject: Please attend conference call to discuss CDC positions on thimerosal containing vaccines

in preparation for the October 20-22 ACIP meeting. Roger Bernier requested I set up this call.

Please let me know which of these times DO NOT work for you to attend the call, and if you think others should be invited to it, let me know that as well. We will plan for a one hour call, but can go over if necessary, and I will set up a conference call bridge for those attending.

Tuesday, Oct. 5: 10-12

2-4

Wednesday, Oct. 6 10-12

The specific objectives of the call are to develop a CDC consensus, or a process for consensus on the following issues, ideally to be ready for presentation to the ACIP:

1. Should there be any further changes to the recommendations for hepatitis B vaccination of infants?
2. Should CDC recommend a preference for use of thimerosal-free DTP vaccines?
3. Should CDC recommend a preference for use of thimerosal-free Hib vaccines?
4. Develop language for a draft Notice to Readers on continuing to recommend influenza vaccine, despite presence of thimerosal, for high-risk children, and pregnant women, that could be used for interim guidance by CDC staff, pending ACIP decision on the matter.

Many of you were involved in recent detailed verbal and e-mail discussions on the last issue. To help focus that discussion, I will attempt to summarize the pertinent varying points of view from e-mails, with the author(s) attributed

in parentheses. Please correct me or elaborate if the points are not clear, by return e-mail or at the call itself, since I did not quote some entire messages, but what appeared to be the most cogent points. The major question appears to be can or should CDC/ACIP develop a Notice about use of influenza vaccine containing thimerosal that is very brief, with no or very few data, and then shortly thereafter publish a more detailed document with all the relevant data, or are these two concepts inseparable?

If we decide that more time for this discussion and further review of data is necessary, as Dixie Snider and Tom Sinks suggest in the first two notes below, we can schedule that as well, if necessary, but for now we are aiming at the interim guidance I noted above.

General:

I still don't think we are using the data on "permissible" methyl mercury exposure levels to properly assess risk. The whole issue of relating what we're giving in vaccines to their impact on blood and tissue levels of Hg rather than relating them to the chronic exposure standards of ATSDR, EPA, etc. seems to have not been something that we have been able or willing to delve into. Until we do that, I don't think we're analyzing the situation appropriately.

Bottom line - I would like to see NCID, NVPO, NIP, and NCEH develop a deliberative process and report the outcome in an appropriate medium. However, until that is done, it is a fact that CDC, ACIP, and AAP have not changed their recommendations regarding administration of flu vaccine and I think that can be said in several venues without having a special article at this time.

(Snider)

... if there is a need to look specifically at the issue of thimerosal and pregnant women and infants getting influenza, we should do this in such a way that can be referred to. I think Dixie also supported this. If it were me, I would bring together a few knowledgeable people and sorting through the possibilities for using the vaccine versus what we know and don't know re thimerosal. I think a 1/2 day or day to go over the issues, make some calculations, and develop a position paper on this would be the way to go. You could then refer to the process and defend it to anyone who wanted to criticize it. I would suggest someone from ATSDR, myself and Ed, George Lucier from NTP, and Bern Schwetz from FDA to handle the Hg risk side and some vaccine and influenza people to handle the benefit and situation side: (Sinks)

Suggested partial rewrite and approach by Ed Kilbourne:

"Like many childhood vaccines, Influenza vaccines contain thimerosal as a preservative. Despite the lack of any specific data documenting harm from the very small quantities of preservative present, it has been judged prudent to develop thimerosal-free vaccines, and vaccine companies have already started to do so. Although this year's vaccines do contain thimerosal, the documented, severe health consequences from failure to vaccinate far outweigh any possible risk from thimerosal. Accordingly, the (ACIP) recommendations regarding who should receive influenza vaccination are unmodified."

And that's all I would say. I would not go into a quantitative analysis comparing the exposure with the ATSDR MRL or analogous numbers put forth by other agencies. I would not go into safety margins, which are debatable. I would not go into differences between fetal and adult brains. And I certainly would not center the whole communication around the thimerosal issue. Ultimately, what you hope to address is the overall public health problem. The concern of substance is influenza, not possible ill effects of thimerosal. The article should reflect those priorities in approach. (Kilbourne)

Notice was [originally] intended to let people know there were no changes in recommendations. It was not to revisit the issue of what is "acceptable" based on what evidence (or lack thereof). (Fukuda)

Influenza vaccination of high risk children:

"The risks of not vaccinating high-risk children far outweigh the unknown and probably much smaller risk, if any, of neurodevelopmental effects posed by exposure to thimerosal-containing vaccines." How can you say this if it is unknown? While the risks of not immunizing children may be clear, the risks of thimerosal are uncertain - your statement is too strong. (Sinks)

"There are no data or evidence of any harm caused by the level of exposure that some children may have encountered in following the existing immunization schedule." *Nor is there any evidence that it doesn't pose a risk - because nobody has looked - aren't there some studies showing increased exposure to Hg following immunization with Hep B? (Sinks)*

Influenza vaccination of pregnant women:

I would feel much better if you could share the actual numbers that were persuasive to you all in crafting the statement (Dowell)

I think this needs to be more quantitative and should reflect the uncertainty that exists. At least mention that you are basing these conclusions on what is known about oral ingestion of methyl Hg or see the language we worked upon for the last notification on Hep B vaccine. (Sinks)

Perhaps some wording to the effect that the mercury exposure from a flu vaccine would be less than (?a week's dietary intake for a woman who eats fish once a week?) or some such statement at the end of the third paragraph would put the issue in perspective. (Dowell, Walt Orenstein, perhaps others)

"The chronic, daily mercury ingestion reported [in several studies - primarily Seychelles study] greatly exceeds the amount of mercury that a pregnant woman would receive from a single annual dose of thimerosal-containing influenza vaccine."
[This] sentence might well be deleted. I don't think it adds anything and, in some ways is misleading. I am not sure that I would want to argue, for example, that one could take the allowed amount of mercury for a year and administer it as a bolus injection with the same outcome as having has it spaced out evenly over the year; the issue then becomes one of how much of a bolus can one give at one time without harmful effect and this data does not exist (or at least I'm not aware of them). (Egan, FDA)

In order to prepare such a statement that CDC folks can be comfortable with, we should redraft the notice to readers to contain more information about Hg blood levels that a pregnant woman might experience as a result of flu vaccination and why such levels are judged safe. (Bernier [for NIP].

END

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