Tom, what do you think?
-----Original Message-----
From: EMiller@phls.org.uk [mailto:EMiller@phls.org.uk]
Sent: Tuesday, June 26, 2001 11:25 AM
To: rtcl0@cdc.gov
Subject: RE: UK vaccine schedule and thimerosal exposure

Dear Bob

The information given to me by the licensing authority is that the whole cell DTP/Hib vaccine we currently use contains 50 micrograms thimerosal per dose so that our children would if on schedule have 75 micrograms of ethyl Hg by 4 months of age. They originally told me that the whole cell DTP vaccine that we used on its own from 1990 (when we adopted our accelerated schedule) up to 1992/3 contained 100 micrograms thimerosal so exposure to ethyl Hg would have been 150 ug by 4 months. We then started using combined DTP/Hib vaccines for which the thimerosal content apparently was 50ug /dose. The authority is now saying that they may have made a mistake and the vaccine we used up to 1992/3 only contained 50ug thimerosal /dose! If this is true then do we have sufficient exposure to ethyl Hg by 4-6 months of age to pick up an effect? Do I have to give my GPRD grant money from WHO back???

Liz

-----Original Message-----
X-Sybari-Trust: 44falcsf 050014dd 00000000 00000030
From: rtcl0@cdc.gov [mailto:rtcl0@cdc.gov]
Sent: 26 June 2001 14:50
To: EMiller@phls.org.uk
Subject: UK vaccine schedule and thimerosal exposure

Liz,

In our brief discussions in Geneva, did I recall correctly that you said the vaccines used in the UK contained 50 micrograms thimerosal (or 25 micrograms ethyl Hg) per dose? If this is correct, at the end of 3 doses at 4 months of age, the exposure would have been to 150 micrograms of thimerosal or 75 microgram ethyl Hg. The range of exposures at 4-5 months of age (after the 2nd dose of DTP, Hib and Hep B) in the VSD study was from 150-250 micrograms of thimerosal or 75-125 micrograms of ethyl Hg.

We look forward to hearing more about your study with Jean Golding's cohort.

Best regards,

Bob

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The licensing authority has now definitively confirmed that the whole cell vaccine we used prior to 1996 did only contain the 50ug thiomersal dose. This is really annoying as we checked with them several times. I will need to discuss the implications of this with WHO. What is the thiomersal exposure in the Harald Heibel study because I believe they used the UK whole cell vaccine for their 2 4 6 vs 3 5 12 month so even with the most accelerated schedule the Swedish children would get less exposure than our kids routinely get. What do you know about this study design? We still have the opportunity of using another cohort (the one I briefly mentioned) for which there is much more detailed quantitative information on development and much more information on potential confounders. The exposure would be the same - max 75 ug ethyl hg by 4 months.

Liz

-----Original Message-----
From: rttcl@cdc.gov [mailto:rttcl@cdc.gov]
Sent: 26 June 2001 22:47
To: EMiller@phls.org.uk
Subject: FW: UK vaccine schedule and thiomersal exposure

Liz, FYI.

-----Original Message-----
From: Verstraeten, Thomas Sent: Tuesday, June 26, 2001 12:05 PM
To: Chen, Robert (Bob) (NIP)
Subject: RE: UK vaccine schedule and thiomersal exposure

Bob,
I think two issues are important in assessing the potential strength of the GPRD study:

1. Maximum exposure and 2. Unbiased controls

The maximum exposure is indeed relatively low if that was the only T containing vaccine used. My estimate would be that you need at least >50 by 3 months or >100 by 6 months to see an effect if there is one, which you barely make (50 at 2 mo and 75 at 4 mo in the UK)

The quality of the comparison group is maybe even more important if you consider all the criticism we have received on comparing high T exposure to no or low T exposure. I'm not sure if the GPRD is that reliable that you can be sure that low exposure is really low exposure and not underascertainment in the database.

I hate to say this, but given these concerns, it may not be worth doing this after all. On the other hand, maybe the grant can be given to Harald in Sweden to do his follow-up of the Diap trial kids...

Tom

-----Original Message-----
From: Chen, Robert (Bob) (NIP) Sent: Tuesday, June 26, 2001 11:45 AM
To: Verstraeten, Thomas
Subject: FW: UK vaccine schedule and thiomersal exposure
Dear Bob,

Hope all is well with you and your family. I am just about to receive the QFRD data which we propose to use to do the type of study you did on the VSD data set. It would be very helpful if you had a protocol describing what you did in your study, in particular what the background variables were that you included as possible confounders. I am on leave from 21st August until 10 Sept. but Nick, the statistician who will be working on this data set is around and you could liaise with him directly. Incidentally Nick will be presenting our DPV/intussusception work at the forthcoming Washington meeting and would appreciate a chance to talk to you and Tom (whom I see will also be there) about the thiomersal study. Although we don't have the level of exposure that you had in the US there is such a lot of interest here that this study is becoming increasingly important. I have also got funding to look at the ALSPAC cohort which I believe I sent you the protocol for. This cohort has got detailed behavioural and developmental data available as well as information on other mercury exposures.

With best wishes

Liz

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Dear Bob,

We will shortly be starting our analyses on the GPRD dataset and would be grateful if you or some one at your end could look at the list of conditions we have identified as relevant developmental outcomes (this I am faxing as I do not have it electronically). The codes in the GPRD are Read or Oxmis (Rdxflaf 0 or R) and there is not a precise mapping to ICD 9. We have identified all the codes that we think are relevant to the outcomes of interest and as you will see have flagged them as follows:

1 = child psychoses
2 = specific psychopathological symptoms
3 = emotional disturbance
4 = hyperkinetic syndrome
5 = specific developmental delay
6 = mental retardation

I would be interested if you have any comments. Have we got the right conditions (as judged by the text field) and are there any other conditions that we might have missed?

I dont know what the coding system is for medical conditions on your HMOs but if there is anything similar to the one on the GPRD and if you have a list of the conditions you flagged this would be very helpful to us, not only for the outcomes of interest but also the exclusions and other background conditions that you took account of in the analysis as potential confounders.

Can you let me know if you dont get the fax!

With best wishes

Liz
Dear Bob,

You will recall that I faxed to you a list of medical conditions that we intend to use as the outcome measures in the thiomersal study. I have now got this file in Excel in case you will find it easier to email to your colleagues.

The Sunday Times did run a small piece on the "secret report showing a 2 fold increase in autism rates that was suppressed" even though they were given the truth and know that the content of the piece was entirely misleading.

best wishes

Liz

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