Brockner Ryan, Beth

From: Ball, Leslie
Sent: Thursday, June 10, 1999 3:29 PM
To: Patriarca, Peter
Subject: RE: mercury

Peter:

Thanks for your comments. If you refer to slide 48: "Stakeholders", I briefly mentioned the issue of vaccine supply if thimerosal use was restricted and the cost to manufacturers (and to the public/providers) of implementing a change in formulation as well as thimerosal as "stablizer" in vaccines. These issues will need to be addressed more thoroughly.

Re: thimerosal removal and induction of conformational changes in antigenic determinants, this issue is central to whether the FDA will require additional studies for formulations in which thimerosal is removed. There is a CBER precedent on this issue (for better or worse) with COMVAX in which the pivotal efficacy studies were done with a product containing thimerosal, but the PLA was filed and approved with a product in which the thimerosal was removed. At the pre-PLA meeting (I am trying to retrieve records of this), Merck was apparently told that no further clinical studies were necessary on the product without thimerosal, and that manufacturing bridging was all that was necessry. Karen Midthun's recollection was that this was a decision by the product reviewers. Any further light you can shed on this decision, and its applicability to other products, would be helpful.

Re: your comment on the risk of contamination if thimerosal is removed, Neal Halsey is putting together a manuscript from the workshop held at Hopkins 9 months ago on injection guidelines that concludes that unidose vials are the best option to avoid contamination and prevent medication errors. (As you recall, thimerosal did not prevent the occurrence of abscesses following DTP vaccine from multidose vials.) At the time Dr. Halsey wasn't even considering the advantage of unidose vials if thimerosal is removed. Bill Egan has checked with Mark Raza on whether the FDA is compelled to follow USP standards for preservatives and it apprears we are not.

In any event, I think the way to go is to move to single dose vials. CDC (Bob Snyder) told me last fall that this would not be a problem for clinics depending on federal purchases if unidose vials were phased in gradually. Obviously, more discussion needs to go into this issue.

Thanks for your insight.

Leslie