

Brockner Ryan, Beth

From: Baylor, Norman
Sent: Saturday, July 03, 1999 4:21 PM
To: Ball, Leslie; Goldenthal, Karen; Pratt, Douglas R.; Deal, Carolyn D.; Weir, Jerry P.; Esber, Elaine
Subject: FW: A potential solution...

See below.

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

From: Livengood, John [SMTP:jrl1@cdc.gov]
Sent: Saturday, July 03, 1999 3:23 PM
To: Evans, Geoffrey (HRSA); 'marty home'; Baylor, Norman W. (FDA); Rabinovich, Regina (NIH)
Subject: FW: A potential solution...

> -----Original Message-----

> From: Schwartz, Ben (NIP)
> Sent: Saturday, July 03, 1999 8:19 AM
> To: Cordero, Jose; Bernier, Roger; Pless, Robert; Nowak, Glen;
> Livengood, John; Myers, Martin G.; Evans, Geoffrey (HRSA)
> Cc: Hibbs, Beth; Broom, William L.; Chen, Robert (Bob) (NIP); Rodewald,
> Lance
> Subject: A potential solution...

> Folks:

> Below and attached is one potential approach to address the thimerosal
> problem. I think that this approach is scientifically valid, overcomes
> the communications problems, and could be acceptable to pediatricians and
> the public. As a parent of a 3-month old, I was very uncomfortable with
> the good vaccine/bad vaccine dichotomy and would have been reluctant to
> accept a thimerosal containing product for my baby. Given the approach
> presented below, I would be very comfortable knowing that my child would
> receive a thimerosal containing product as long as the defined safe cutoff
> for mercury is not exceeded. (See additional comments, below the
> attachment and text copy).

> <<thimerosal.wpd>>

> Introduction

> The key issue to consider is not whether a vaccine contains thimerosal as
> there is no inherent value in whether or not this is present or in whether
> an infant receives any vaccine that contains thimerosal or has a mercury
> exposure of zero. The focus should not be on what the vaccines do or do
> not contain but rather on whether a child is being exposed to a level of
> mercury that is defined as being potentially harmful. By focusing on the
> child and not the vaccine one can address the most important issue to both
> the pediatrician and the parent: protecting the child both from disease
> and from any potential toxicity.

> The acceptable levels for mercury are defined by the EPA and WHO as levels
> below which there is no risk (or minimal likelihood) of mercury toxicity.
> Although these levels were defined for exposure to methyl mercury, data
> suggest similar toxicities for methyl and ethyl mercury, the form present
> in thimerosal. In fact, the defined cutoffs were established with a
> substantial margin of safety built in to assure that no toxicity occurs.
> Within the first 6 months of life, for a child of average weight, both WHO
> and EPA define this cutoff as a cumulative exposure of about 100 ug. By
> two years of age, a cumulative exposure to about 550 ug is acceptable for
> a child of average weight. Note that both ATSDR and the FDA define 3- and
> 4-fold higher levels of exposure, respectively, as acceptable.

> Goals

- > 2. Assure that exposure to mercury does not exceed EPA and WHO defined cutoffs for cumulative exposure, especially within the first 6 months of life.
- >
- > 3. Maintain the ability of the immunization program to provide safe vaccination regimens to all children in both the private and public sectors.
- >
- > 4. Maintain public and provider confidence in the safety of the vaccination program.
- >
- > Approach .
- > Vaccination providers should be instructed to provide a combination of vaccines that will result in complete immunization of infants while not exceeding the accepted, safe level of mercury exposure. There are several options for accomplishing this, with only minimal changes in the vaccination schedule:
- >
- > Vaccinate a child who is not at high risk for hepatitis B (e.g., not born to a surface antigen positive mother or with household exposure to hepatitis B) with a thimerosal containing hepatitis B vaccine at 2, 4, and 12 months. This small change in the vaccination schedule is unlikely to decrease protection (and may actually improve immunogenicity as boosting is greater with a longer interval between doses). Because the concentration of thimerosal in hepatitis B vaccines is lower than other products, the cumulative dose in <6 month old children who receive 2-doses would be 25 ug.
- >
- > • Vaccinate a child with either a thimerosal containing DTaP and a thimerosal free Hib or vice versa. There is one thimerosal free DTaP (Infanrix) and 3 thimerosal free Hib vaccines (ActHIB, PedvaxHIB [liquid], and Comvax which also contains hepatitis B vaccine). The cumulative exposure in <6 month-old children would be 75 ug, or 50 ug if the Merck 2-dose Hib vaccine were used with Infanrix.
- >
- > For an infant at high risk of hepatitis B, provide the first dose of thimerosal containing hepatitis B vaccine at birth, followed by 2-doses of Comvax at 2 and 4 months, and thimerosal containing DtaP for a cumulative exposure in <6 month old children of 87.5 ug.
- >
- > No IPV vaccines contain thimerosal so that this vaccine would not contribute any mercury exposure.
- >
- > Given the above scenarios, the cumulative exposure for a fully immunized child would range between 75 ug and 100 ug, both within the defined safe level of cumulative exposure for a 6 month old child. Moreover, allowing vaccine providers to combine a variety of vaccines to assure a safe cumulative exposure would provide flexibility and minimize the potential for product shortages.
- >
- > Communications
- > When the focus of the communication was on the vaccine product rather than the child, there was an inherent contradiction: why are we moving to thimerosal free vaccines if vaccines containing this product are safe?
- > Parents inevitably would want vaccines that don't contain thimerosal, leading to shortages, deferral of vaccination, and receipt of mercury concentrations that exceed the cutoff by some children. The communication problem is avoided by presenting child-focused messages.
- >
- > Key communications message:
- > Physicians and parents all want to protect children from threats to their health. On-time vaccinations protect children from serious diseases such as Hib meningitis and pertussis (whooping cough). Every child can receive all recommended vaccines, some of which may contain thimerosal, and not be exposed to mercury levels that exceed the level defined by EPA and WHO as safe. In fact, this level was chosen with a very wide margin of safety so that the possibility of an adverse effect would be very remote.
- >
- > The concept of a safe level of exposure is one that is familiar both to physicians and to the public. For example, physicians test children

- > for blood lead levels and only intervene (e.g., with chelation therapy)
- > when the level exceeds a defined cutoff. For other heavy metals, such as
- > zinc or cadmium, physicians would only become concerned when a child's
- > exposure exceeded a defined cutoff. For the public also, the idea that
- > there is a level below which no harmful effects occur also makes sense.
- > People choose to eat tuna and other products that contain low levels of
- > mercury because they know that this level of exposure will not result in
- > any toxicity.
- >
- > If vaccinations can be completely and safely given now, why is the FDA
- > encouraging vaccine manufacturers to remove thimerosal from their
- > products? One answer is that by increasing the number of thimerosal free
- > products, it will be easier for vaccine providers to purchase and provide
- > vaccines. Currently, there are some regimens that would exceed defined
- > cutoffs. When more products are thimerosal free, physicians will have
- > more flexibility and it will be easier to assure that no child receives a
- > regimen that could possibly result in some toxicity. Moreover, by
- > increasing flexibility, the possibility of shortages would be decreased
- > assuring that all children are able to receive needed immunizations.
- > Also, greater availability of thimerosal free products would further
- > increase the margin of safety, particularly for premature and low birth
- > weight infants for whom the defined cutoff may be lower. Finally, this
- > change would reassure the public that the PHS and vaccine manufacturers
- > are continuing to do whatever possible to assure optimal safety and
- > maintain public confidence in the vaccination program.
- >
- > This approach also would protect vaccination programs in the developing
- > world. It would be possible to provide all recommended vaccines,
- > including Hib and hepatitis B without exceeding the defined cutoff or, if
- > this cutoff is exceeded, still remaining well within the margin of safety.
- > In the developing world, where the risk of mortality or severe morbidity
- > from vaccine preventable diseases is much greater, the balance between the
- > risks associated with non-vaccination and exposure to a mercury level that
- > is below the cutoff or within a safe margin of that cutoff is clearly in
- > favor of vaccination. By focusing on the child, rather than defining a
- > specific vaccine product as being better or worse, one avoids the problem
- > of having to avoid certain products. This is particularly important
- > because inclusion of thimerosal prevents contamination of multi-dose vials
- > and is important to protect against potentially severe bacterial
- > infections occurring with contaminated vaccine.
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- >
- > In considering this approach, I would identify two potential problems: 1)
- > disagreement about whether any mercury exposure is safe; and 2) whether
- > there are sufficient doses of the thimerosal free products for this to
- > work.
- >
- > With respect to the safe level, one could point to the levels that define
- > lead toxicity and note that the defined safe levels have changed over the
- > years (either as more data became available regarding possible toxicity or
- > as achieving lower levels became more feasible). To defend the "safe
- > level" approach, one would need to refer to the science about what
- > toxicities occur and to rely on the EPA and WHO as appropriately
- > protecting the public against health threats. Buy-in from the toxicology
- > folks would be important. In addition, one could note that there are
- > other products that contain mercury and other allowable exposures so that
- > implicitly, a safe level is recognized. Also, this is not inconsistent
- > with a statement that further research is being done and that we will
- > continue to try to reduce mercury exposure.
- >
- > With respect to product availability, this is an issue that needs to be
- > discussed with the vaccine manufacturers (hopefully they can be contacted
- > on the weekend).
- >
- > Note also that we are preparing 3 documents to support this position: 1) a
- > document on the toxicology of mercury; 2) a document on the risk of
- > disease if vaccination were decreased or deferred; and 3) a document on
- > the importance of preservatives in multi-dose vials of vaccines. The
- > latter two drafts are attached below. The toxicity document will be
- > forwarded to you by Rob Pless.
- >

> I will be back in the office by ~11:00 (after picking up my daughter from
> Girl Scout camp). Feel free to modify the documents or forward them as
> you feel appropriate.

> <<thimerosal_benefit.wpd>> <<thimerosal_risk.wpd>>

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