

FDA

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**IAG CONFERENCE CALL: 28 JUNE 1999**

**TOPIC: USE OF THIOMERSAL IN VACCINES**

**BACKGROUND:**

**I.) Food and Drug Modernization Act of 1997**

Section 413: Food and Drug Administration Study of Mercury Compounds in Drugs and Food (November 21, 1999)

A.) Complete a list of drugs and foods that contain intentionally introduced mercury compounds

1.) Provide a quantitative and qualitative analysis of the mercury compounds in the list

2.) List and analysis of contents should be completed within 2 years after enactment of FDAMA, i.e., November 21, 2001.

B.) Conduct a study of the effect on humans of the use of mercury compounds in nasal sprays

C.) Conduct a study on mercury sales

1.) The Secretary of HHS, acting through the FDA and subject to appropriations, shall conduct or shall contract with the IOM of the NAS to conduct a study of the effect on humans of the use of elemental, organic or inorganic mercury when offered for sale as a drug or dietary supplement

a.) scope of mercury use as drug or dietary supplement

b.) the adverse effects on health of children and other sensitive populations resulting from exposure to, or ingestion or inhalation of mercury when so used

2.) Consultation with EPA, chair of Consumer product safety commission, and the Administrator of the Agency for Toxic Substance and Disease Registry, and any others needed.

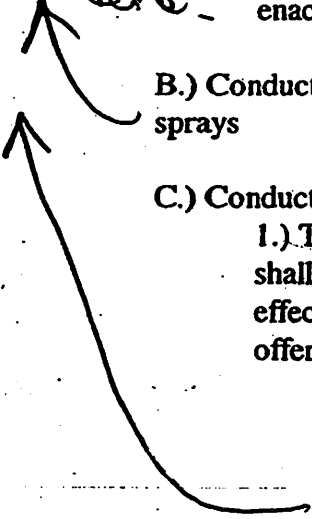
3.) Regulations to be promulgated if data indicate

**II.) FDA Actions**

A.) A working group was formed in FDA to compile the list of products containing mercury compounds

FDA

Any of this done?



- 1.) This list has been completed and analyzed
- 2.) A literature search was completed to examine all published data on the use of mercury compounds in drugs

a.) Drs. Ball and Pratt completed this search for vaccine products

B.) Federal Register notice issued on December 14, 1998, requesting all manufacturers to submit information on drug products containing mercury

1. The following information was requested

a.) Commercial name of products

b.) Mercury compound chemical name

c.) Quantitative amount of the mercury compound in the product (per dose or per quantity of product)

d.) Purpose of the mercury compound in the product (if active, state pharmacological use; if inactive, state the function)

e.) Provide a copy of the product label

f.) State the amount of the mercury compound used annually in manufacturing the product.

### III.) European Agency for the Evaluation of Medicinal Products

#### A.) Working Document from the Multidisciplinary Group on Thiomersal

1.) In Jan/Feb 1998 the Committee for Proprietary Medicinal Products' Biotechnology Working Party circulated a report on the use of thiomersal and other organomercurials as preservative in biopharmaceuticals to the Safety Working Party (SWP) and the CPMP

2.) The SWP examined safety concerns related to the use of thiomersal at their February 1998 meeting and made preliminary recommendations to the CPMP

3.) On 22 April 1998, the CPMP agreed on a concept paper on thiomersal which outlined a multidisciplinary action plan to evaluate the benefit/risk of medicinal products containing thiomersal

4.) On 19 October 1998 and 14 December 1998 multi-disciplinary meetings were held (Quality Working Party, QWP; Biotechnology Working Party, BWP; Safety Working Party, SWP; and Pharmacovigilance Working Party PhWP

FDA knew in Oct '98  
did nothing

## 5.) RECOMMENDATIONS

a.) The presence of thiomersal should be stated on the label

b.) The package insert should contain information regarding the risk of sensitization in relation to thiomersal and other preservatives

c.) For vaccination in infants and toddlers the use of vaccines without thiomersal and other mercurial containing preservative should be encouraged; however, in order not to jeopardize vaccine supplies and immunization programs, it is advisable to introduce requirements for the elimination of organomercurial preservatives in vaccines on a gradual basis

B.) In order to discuss the recommendations of the CPMP Working Document with interested parties, a meeting under the chairmanship of Dr. Mary Teeling, was convened on 19 April 1999.

1.) Attendees: The European Pharmacopeia, WHO, FDA, and relevant manufacturers organizations

2.) Conclusions with respect to vaccines

a.) The European vaccine manufacturers indicated that for new vaccines there is currently a move towards the development of preservative-free vaccines. Where a preservative is needed, the possibility of reducing the level of the preservative is being actively examined. For existing vaccines which are already on the market, manufacturers are looking to re-formulate on a case-by-case basis where feasible, although it was noted that due to the complexity of re-formulating and the time involved the main focus is on new vaccines and combination vaccines

## IV.) FDA's Medical Policy Coordinating Committee Meeting (MPCC)

A.) This is an internal CBER committee composed of medical officers from each product office and from the Office of the Director

1.) Dr. Leslie Ball, CBER/Office of Vaccines Research and Review, was invited to the June meeting to discuss her findings in searching the literature for information on potential adverse effects from thiomersal used in vaccines

2.) Dr. Neal Halsey was also invited to this meeting because he had been approached by Dr. Ball to consider completing studies on the use of thiomersal in vaccines (Dr. Halsey was not invited to the June 1998 MPCC meeting in his capacity as a member of the AAP)

a.) Drs. Ball and Pratt had been in contact with numerous individuals

Ask  
her  
about  
this

within the FDA, CDC, NIH, WHO, and investigators from academic institutions

**V.) CBER's Position**

**A.) As a follow-up to the 14 December 1998 FR notice, all vaccine manufacturers will be requested to provide the Agency with information regarding their plans for thiomersal as a preservative in U.S. licensed vaccines**

**1.) The rationale for the continued use of thiomersal, as well as the feasibility of eliminating or reducing the amount of thiomersal will be requested**

**B.) CBER will continue to work with its IAG, VRBPAC, and WHO colleagues as well as others to study the effects of the use of thiomersal in vaccines on infants and other sensitive populations (e.g., pregnant women), as per our FDAMA mandate,**

**Ellenberg, Susan**

From:  
Sent:  
To:

McLendon, Louann M. [lmm3@cdc.gov]

Friday, June 25, 1999 1:04 PM

Balbier, Thom (HRSA); Baylor, Norman W. (FDA); Benor, David E. (OS); Breiman, Robert; Caserta, Vito (HRSA); Cordero, Jose; Crawford, Shaunette; Curlin, George (NIH); Donlon, Jerome A. (FDA); Egan, William M. (FDA); Ellenberg, Susan (FDA); Esber, Elaine C. (FDA); Evans, Geoffrey (HRSA); Frischer, Ruth; Gerber, Michael; Goodman, Rita A. (HRSA); Graydon, Randy; Heilman, Carole; Hoke, Charles; Hughes, James; LaMontagne, John; Landry, Martin; Landry, Steve; Livengood, John; Mahanes, Joan A. (HCFA); Mahoney, Louis E. (HRSA); Mawle, Alison; Murphy, Rosemarie J. (HCFA); Myers, Martin; Nichols, Bill; Orenstein, Walt; Postema, Alicia; Puryear, Michele (HRSA); Rabinovitch, Regina (NIH); Robinson, Bill A. (HRSA); Schwartz, Benjamin; Sepe, Stephen; Snider, Dixie; Trump, David; Zanca, Jane

Cc:  
Subject:

Sinks, Tom; Patriarca, Peter A. (FDA); Bail, Leslie K. (FDA)  
FW: IAG Conference Call

*Denise*

*L. Bail, Goldenthal,  
R. Ball, D. Ball  
Patriarca, Deal, ?*

> There will be a special IAG conference call on Monday, June  
> 28 at 9:00 am-10:30 am to consider Thimerosal in vaccines.

*Barry McMurry*

> Marty

> This is to confirm that your conference call has been  
> scheduled.

*one-pager for Koplan to  
share with them*

> All conference calls are scheduled on Eastern time.

> Your Conference name: IAG

> Your Conference telephone bridge number : 404-639-4100 or  
> 1-800-713-1971

> For security and confidentiality purposes, participants will  
> not be connected to a conference call without a valid conference code.

> CONFERENCE CODE: 865702

> DATE: 28-June-99

> TIME: 9:00 a.m. - 11:00 a.m.

> PARTICIPANTS: 25

> If you have a problem during your conference, you may press  
> \*0 at anytime to signal the attendant. If you have questions, about the  
> technical operations of the teleconference equipment please call  
> 404-639-7550.

> Vickie Lynch  
> Teleconference Coordinator

*Sinks : some fraction of  
ethyl-mercury may be  
excreted ~~poorly~~ and not  
metabolized, because it is  
water soluble*

*Conservative approach is probably  
warranted at present, w/o  
further data*

*not known how acute exposure  
effects relate to those of chronic  
low-level exposure*

*Dixie Snider concluded about  
urgent meeting of the COI D*

*Reumack says AAP might take action  
tomorrow*

*David suggests a small AB to look at each other's  
product together with management schedule & recommendations*