Review of Thimerosal by the Food and Drug Administration as Required by the Food and Drugs Administration Modernization Act (1997-1999)

Over-the-counter (OTC) products and vaccines are regulated by different branches of the FDA. OTCs are regulated by the Center for Drug Evaluation and Research (CDER). Vaccines are regulated by the Center for Biologics Evaluation and Research (CBER). The FDA's determination that mercury was unsafe and should be removed from over-the-counter medications was published in the Federal Register no fewer than five times prior to the FDA's belated review of mercury in vaccines. What finally prompted the FDA to review mercury in vaccines was not its own regulatory process, but rather an act of Congress. In 1997, Congress passed and the President signed into law, the Food and Drug Administration Modernization Act (FDAMA) of 1997 requiring the study of the "adverse effects on health of children and other sensitive populations from exposure to mercury." At that time the FDA requested information from the pharmaceutical industry and conducted a review of the use of thimerosal in childhood vaccines.

FDA compared exposure levels of infants to ethylmercury from vaccines to existing guidelines for exposure to methylmercury, as there are no existing guidelines for safe exposure to ethylmercury, the metabolite of thimerosal. In 1999, 70 years after the product was first licensed, neither the FDA nor the industry had followed through on determining a safe exposure level to thimerosal or ethylmercury. Thus, when facing a policy decision on thimerosal and vaccines, the FDA had to work from an "assumption"[1] that the toxicity of ingested methylmercury was the same as injected ethylmercury.[2] While this review found no evidence of adverse effects caused by thimerosal in vaccines, except for minor local hypersensitivity reactions, the assessment determined that the use of thimerosal as a preservative in vaccines might result in the intake of mercury during the first six months of life that exceeded recommended guidelines from the Environmental Protection Agency (EPA).

By the time that the FDA conducted its review of mercury in 1999, more than 50 licensed vaccines contained thimerosal. While thimerosal became widely used, there were repeated references in the scientific literature to the lack of substantial understanding of its safety. In numerous publications, researchers suggested that caution be taken in human exposure. For example, a paper published in 1934 noted, "little is known about the mercuric compounds when inoculated into humans. It is therefore preferable to use the minimum amount of this preservative."[3] Unfortunately, when each new vaccine was approved by the FDA and then added to the early infant vaccine schedule by the CDC Advisory Committee for Immunization

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[1] PowerPoint Presentation of William Egan, FDA dated September 14, 1999 http://www.fda.gov/ohrms/dockets/ac/99/backgrd/3544b1f.pdf

[2] It should be noted that it is widely accepted in toxicology that the level of exposure to a toxin through injection which would create an adverse reaction would be much lower than the level of exposure needed to create a similar reaction through ingestion.

[3] ELC002239-57; Rosenstein, Carolyn et.al.; "The Bactericidal and Antiseptic Action of Preservatives Frequently Used in Biological Products, and the Effect of these Preservatives on the Potencies of These Products;" The American Journal of Hygiene; September 31, 1934.

Practices (ACIP) none of the committee members, the CDC National Immunization Program or the FDA Center for Biologics Evaluation and Research had determined cumulative mercury exposure levels. The essence of the debate was captured in a 1999 e-mail from a former FDA official weighing the pros and cons of taking action. He opined that hastening the removal of thimerosal from vaccines would: *"…raise questions about FDA being 'asleep at the switch' for decades by allowing a potentially hazardous compound to remain in many childhood vaccines, and not forcing manufacturers to exclude it from new products. It will also raise questions about various advisory bodies regarding aggressive recommendations for use. (We must keep in mind that the dose of ethylmercury was not generated by "rocket science". Conversion of the percentage thimerosal to actual micrograms of mercury involves ninth grade algebra. What took the FDA so long to do the calculations? Why didn't CDC and the advisory bodies do these calculations when they rapidly the childhood immunization schedule?)"*[4] *Email from Dr. Peter Patriarca, Director, Division of Viral Products, Food and Drug Administration, to Martin Meyers, Acting Director, National Vaccine Program Office, Centers for Disease Control and Prevention.(June 29, 1999)

Dr. Neal Halsey, Director of the Institute of Vaccine Safety at Johns Hopkins University was an influential member of Federal advisory committees that oversaw the expansion of the Federally-recommended schedule of childhood vaccines in the 1990s. By all accounts, Dr. Halsey was instrumental in the decision to seek the removal of Thimerosal from childhood vaccines in 1999. Dr. Halsey told the New York Times that he was astonished when he reviewed an FDA analysis of how much mercury was in vaccines being given to children: *"My first reaction was simply disbelief, which was the reaction of almost everybody involved in vaccines. In most vaccine containers, thimerosal is listed as a mercury derivative, a hundredth of a percent. And what I believed, and what everybody else believed, was that it was truly a trace, a biologically-insignificant amount. My honest belief is that if the labels had had the mercury content in micrograms, this would have been uncovered years ago. But the fact is, no one did the calculation." "My first concern was that it would harm the credibility of the immunization program. But gradually it came home to me that maybe there was some real risk to the children."*[5]

On July 9, 1999, the American Academy of Pediatrics joined the U.S. Public Health Service in issuing a joint statement recommending the removal of all thimerosal from vaccines. On its website, the FDA provides the following rationale for its policy on thimerosal: *"Over the past several years, because of an increasing awareness of the theoretical potential for neurotoxicity of even low levels of organomercurials, and because of the increased number of thimerosal-containing vaccines that have been added to the infant immunization schedule, concerns about the use of thimerosal in vaccines and other products have been raised. Indeed, because of these concerns, the Food and Drug Administration has worked with, and continues to work with, vaccine manufacturers to reduce or eliminate thimerosal from vaccines."*[6] The FDA was criticized by some in 1999 for not taking more forceful action to remove thimerosal. As a

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[4] Email from Dr. Peter Patriarca, Director, Division of Viral Products, Food and Drug Administration, to Martin Meyers, Acting Director, National Vaccine Program Office, Centers for Disease Control and Prevention.(June 29, 1999) .

[5] Allen, Arthur; "The Not-So-Crackpot Autism Theory;" The New York Times Sunday Magazine; November 10, 2002.

[6] http://www.fda.gov/cber/vaccine/thimerosal.htm#intro

result of the FDA decision to seek a gradual removal, many children continued to receive injections of the DTaP, Hib, and Hepatitis B vaccine that contained mercury well into 2001. Mercury-containing vaccines manufactured in the United States, up to today, continue to be administered to infants and small children in the United States and abroad.