

# Thimerisol:

## 1. Why is thimerosal used as a preservative in some vaccines?

Thimerosal is used as a preservative in some multi-dose vials of vaccines to prevent contamination. Preservatives are not required for vaccines in single-dose vials. As a preservative, thimerosal is added at the end of the production process to the bulk or final container to prevent contamination after multi-dose vials are opened. Until 1999, vaccines given to infants to protect them against diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b (Hib), and Hepatitis B contained thimerosal as a preservative. Today, with the exception of some flu vaccines, none of the vaccines used in the U.S. to protect preschool aged children against 12 infectious diseases contain thimerosal as a preservative. Thimerosal still may be used in the early stages of manufacturing of certain vaccines, but is removed through a purification process, with only trace, or insignificant, amounts remaining.

## 2. If thimerosal was used in vaccines for many years, why did it become a concern?

The Food and Drug Administration (FDA) Modernization Act of 1997 called for the FDA to review and assess the risk of *all* mercury containing food and drugs. As part of this effort, the FDA conducted a review of mercury content in vaccines.

## 3. What recommendations did the Federal government make in 1999 with respect to thimerosal in vaccines?

A review conducted by the Food and Drug Administration (FDA) concluded that the use of thimerosal as a preservative in vaccines might result in the intake of mercury during the first 6 months of life that exceeds the Environmental Protection Agency (EPA), but not the FDA, the Agency for Toxic Substances and Disease Registry (ATSDR), or the World Health Organization (WHO) guidelines for *methylmercury* intake (Ball et al., 2001). Thimerosal contains *ethylmercury*. Methylmercury is a related compound and has been more thoroughly researched than ethylmercury. Thus, federal safety standards are based on information we have about methylmercury.

FDA's review found no evidence of harm caused by doses of thimerosal in vaccines, except for minor local reactions (Ball et al., 2001). Nevertheless, in July 1999 the Public Health Service agencies (PHS), the American Academy of Pediatrics (AAP), and vaccine manufacturers agreed that thimerosal levels in vaccines should be reduced or eliminated as a precautionary measure, and the Food and Drug Administration (FDA) committed to expediting the review of new vaccines that do not contain thimerosal.

## 4. What progress has been made since July 1999 in removing thimerosal from vaccines routinely recommended for infants?

Substantial progress has been made in the effort to reduce thimerosal exposure from vaccines. Today, with the exception of some flu vaccines, none of the vaccines used in the U.S. to protect preschool aged children against 12 infectious diseases contain thimerosal as a preservative. The vaccines with trace amount of thimerosal licensed to date contain less than 0.5 micrograms of mercury per dose, that is, a given dose of vaccine contains less than 1 part per million.

Events that contributed to accomplishing this goal include the licensure of a thimerosal free Hepatitis B Vaccine (Recombinant) manufactured by Merck and Company in August 1999. FDA licensed another hepatitis B vaccine with only trace

amounts of thimerosal, manufactured by GlaxoSmithKline in March 2000. A supplement for a new formulation of Aventis Pasteur's DTaP Vaccine with only a trace amount of thimerosal was approved in March 2001. Additionally, Wyeth-Lederle Vaccines and Pediatrics now only markets a single-dose, thimerosal-free formulation of its Haemophilus b (Hib) Conjugate Vaccine in the U.S. Thus, two hepatitis B vaccines are thimerosal free, four Hib vaccines are thimerosal free, and two DTaP vaccines are thimerosal free.

Prior to the recent initiative to reduce or eliminate thimerosal from childhood vaccines, the maximum cumulative exposure to mercury via routine childhood vaccinations during the first six months of life was 187.5 micrograms. With the newly formulated vaccines, the maximum cumulative exposure during the first six months of life will now be less than three micrograms of mercury; this represents a greater than 98 percent reduction in the amount of mercury a child would receive from vaccines in the first six months of life. [Influenza (flu) vaccine is not given until six months or older.

**5. I've heard that children may be getting toxic levels of mercury from vaccines. Is that true?**

No. There is no evidence of harm caused by the minute doses of thimerosal in vaccines, except for minor effects like swelling and redness at the injection site due to sensitivity to thimerosal.

Most importantly, since 1999, newly formulated thimerosal preservative-free vaccines have been licensed. With the newly formulated vaccines, the maximum cumulative exposure during the first six months of life will now be less than three micrograms of mercury. No children are receiving toxic levels of mercury from vaccines.

**6. What research is being conducted by the Federal Government regarding the safety of vaccines containing thimerosal?**

There is no evidence to suggest that thimerosal in vaccines causes any health problems in children and adults beyond local hypersensitivity reactions (like redness and swelling at the injection site). However, efforts to remove thimerosal from the U.S. vaccine supply have been accompanied by research investigations to better assess the potential health effects of exposure to thimerosal containing vaccines:

- The National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health (NIH) funds thimerosal research that focuses on better understanding of what happens to thimerosal once it is introduced into the body and how this compares to current knowledge of methyl mercury pathways.
  - A recent study sponsored by the NIAID and conducted at the University of Rochester assessed mercury levels in 40 infants who received vaccines containing thimerosal and 21 infants who received thimerosal-free vaccines. The scientists measured the level of mercury in the infants' blood, urine and stool up to 28 days after vaccination. They found that 1) infants who were given vaccines with thimerosal had levels of mercury well below the safe level of 29 nmol/L (this level is set ten times lower than the level at which mercury begins to cause neurological problems) and 2) the body seems to be able to get rid of thimerosal (ethyl mercury) via the gastrointestinal tract (stools) much quicker than it gets rid of methyl mercury. For more information about the different types of mercury go to <http://www.cdc.gov/nip/vacsafe/concerns/thimerosal/faqs-mercury.htm>
  - NIAID and the National Institutes of Environmental Health Sciences (NIEHS) are also funding studies comparing the pharmacokinetics and tissue distribution of thimerosal, ethyl mercury, and methyl mercury in non-human primates. Pharmacokinetics is the study of how an agent is absorbed, distributed, metabolized (broken down), and excreted. For more information go to <http://www.niaid.nih.gov/factsheets/thimerosal.htm>
- The Food and Drug Administration (FDA) has been actively addressing the issue of

thimerosal as a preservative in vaccines. For information on FDA activities related to thimerosal and vaccines go to <http://www.fda.gov/cber/vaccine/thimerosal.htm>

- See also [CDC studies on the safety of thimerosal-containing vaccines](#).
- The CDC's Center for Environmental Health and the National Center for Health Statistics are doing a study looking at all mercury exposures and working with the National Health and Nutrition Examination Survey (NHANES). NHANES 4 will collect samples of blood, hair and urine from all women of reproductive age and children under 5 in order to assess mercury levels in the body from all sources of mercury a person can be exposed to in the environment. Findings of a study conducted using NHANES 3 data to check blood and hair mercury levels suggest that the mercury levels in young children and in women of childbearing age are generally below the level considered hazardous (MMWR;50, 140-143).

## 7. Does thimerosal cause autism?

There is no conclusive evidence that any vaccine or vaccine additive increases the risk of developing autism or any other behavior disorder. Rather, evidence is accumulating of lack of any harm resulting from exposure to vaccine containing-thimerosal as a preservative. In a 2004 report, the Institute of Medicine (IOM) concluded that there is no association between autism and vaccines that contain thimerosal as a preservative. Nonetheless, given the level of concern among parents and others regarding vaccines and autism, the CDC is committed to investigating this issue to the fullest extent possible, using the best scientific methods available.

For more information on autism and vaccines go to [www.cdc.gov/nip/vacsafe/concerns/autism/default.htm](http://www.cdc.gov/nip/vacsafe/concerns/autism/default.htm)

## 8. What about a 2003 study that claimed to find a relationship between thimerosal in vaccines and autism, speech disorders, and heart disease?

In 2003, Geier and Geier reported conducting two analyses to test whether thimerosal in vaccines is associated with autism, speech disorders, and heart disease. The researchers inadequately described the methods they used, making it impossible to determine exactly what was done and how the results should be interpreted. In the first analysis, the researchers reviewed Vaccine Adverse Event Reporting System (VAERS) reports involving autism, speech disorders, and heart disease. They state that they compared VAERS reports involving thimerosal-containing DTP and DTaP vaccines with those involving thimerosal-free DTaP vaccines. There are a number of weaknesses in this analysis, including an apparent misunderstanding among the authors regarding VAERS reporting requirements. VAERS is a passive surveillance system for reporting possible vaccine adverse events that depends on health care providers, patients, and/or others to file reports. Health effects reported to VAERS as following vaccination may be true adverse events, coincidental occurrences, or mistakes in filing. Because of this, VAERS has certain weaknesses that limit the system, including incomplete reporting, lack of verification of diagnoses, and lack of data on those who were vaccinated and did not report problems. VAERS data are useful for "hypothesis generation" (raising questions), but should not be used for research aimed at determining whether vaccines cause certain health problems as done by Geier and Geier. Moreover, children who could have received thimerosal-free DTaP vaccine were less likely to have autism or speech disorders diagnosed because they were younger than the children in the thimerosal-containing vaccines group. In the heart disease evaluation, the authors examined reports coded as "heart arrest," these cases in VAERS are completely different from the coronary heart disease cases in the studies that the authors cite to support a possible association between mercury and heart disease. It is also unclear how the researchers calculated levels of mercury exposure, because their calculations are inconsistent with the known levels of mercury that were in thimerosal-containing DTP or DTaP vaccines.

In the second analysis, the authors looked at the estimated amount of mercury exposure from vaccines over time and the number of children enrolled in U.S. special education programs for selected disabilities. The authors present figures with very high correlations, but from the limited description provided, it does not seem that the appropriate data were available to perform the analyses and derive the conclusions that the authors report. Although enrollment in special education of children with autism did increase during the 1990's, it has not been determined whether this represents a real increase in the incidence of autism as opposed to increased awareness and acceptance of the diagnosis, better recognition, changing diagnostic criteria, or educational and service incentives to make the diagnosis.

The American Academy of Pediatrics has more information on this study at <http://www.aap.org/profed/thimaut-may03.htm>.

**9. Great Britain experienced a rapid rise in autism among children born in the 1980's and early 1990's. Could this be due to thimerosal in vaccines?**

It is unlikely that the rapid increase in autism cases in the UK was due to thimerosal. The only vaccine in the UK's childhood immunization program that contains thimerosal is DTP. All other vaccines (OPV, BCG, MMR, Hib, menC) added to the program since the 1950's are and have always been thimerosal free. In addition, if thimerosal in vaccines were causing autism, we would expect to see a simultaneous increase in both thimerosal exposure and autism cases. However, from the 1950's on, there was no increase in the amount of thimerosal UK children were receiving from vaccines, yet there was a jump in autism cases in the 1980's.

A significant change in the UK's program did occur in 1990 when they accelerated their immunization schedule so vaccines would be given earlier (changed from 3, 5, and 8 months to 2, 3 and 4 months). However, the rate of autism was rising long before this change occurred (see Fombonne, 2001).

**10. I understand some people are sensitive to mercury and must avoid it. Do they have problems with thimerosal-containing vaccines?**

Some individuals experience local skin reactions such as redness and swelling that may suggest a delayed-type of minor allergic reaction following injection with products containing thimerosal. Research suggests that most people who have a contact or skin allergy to thimerosal will not have the reaction when thimerosal is injected under the skin (Forstrom, 1980; Jacobs 1982). A prior history of a minor reaction to thimerosal in a vaccine is not considered a contraindication to further vaccination with thimerosal-containing vaccines. Severe anaphylactic (allergic) reaction to any vaccine is a contraindication to further vaccination with the vaccine.

**11. Do measles, mumps, and rubella (MMR) vaccines contain thimerosal?**

No, MMR vaccine does not and never did contain thimerosal. Varicella (chickenpox), inactivated polio (IPV), and pneumococcal conjugate vaccines have also never contained thimerosal.

**12. Do all flu vaccines contain thimerosal?**

No. Influenza vaccine is currently available both with thimerosal as a preservative and preservative-free. For the 2004-05 influenza season, it is likely that 6-8 million doses of inactivated influenza vaccine without thimerosal as a preservative will be available. This represents a substantial increase in the available amount of inactivated influenza vaccine without thimerosal as a preservative, compared with about 3.2 million doses that were available during the 2003-04 influenza season.

The removal of thimerosal as a preservative from influenza vaccine is a complicated process. The total amount of flu vaccine without thimerosal as a preservative will be

increased as vaccine manufacturing capabilities are expanded. In the meantime, it is important to keep in mind that the benefits of influenza vaccination outweigh the theoretical risk, if any, for exposure to thimerosal. Each year, an average of about 36,000 people in the United States die from influenza, and 114,000 have to be admitted to the hospital as a result of influenza. People age 65 years and older, people of any age with chronic medical conditions, and very young children are more likely to get complications from influenza.

### **13. Why are chemicals and other substances added to vaccines?**

Many foods and medicines, including vaccines, have chemicals added to them to prevent the growth of germs, reduce spoilage, and prevent it from losing its potency over time.

Some additives are used in the production of vaccines. Vaccines may include suspending fluid (e.g., sterile water, saline, or fluids containing protein); preservatives and stabilizers (e.g., albumin, phenols, and glycine); and adjuvants, or enhancers, that help the vaccine improve its immunogenicity (ability to protect against disease).

For more information on additives, go to:

<http://www.cdc.gov/nip/vacsafe/concerns/gen/additives.htm>

### **14. How can I find out what chemical additives are in specific vaccines?**

Ask your healthcare provider or pharmacist for a copy of the vaccine package insert. The package insert lists ingredients in the vaccine and discusses any known adverse reactions.