



**Testimony**  
**Before the Subcommittee on Human Rights and**  
**Wellness**  
**Committee on Government Reform**  
**United States House of Representatives**

**CDC's Vaccine Safety Research**  
**Activities**

*Statement of*

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Good morning. I am Dr. Melinda Wharton, Acting Deputy Director of the National Immunization Program at the Centers for Disease Control and Prevention (CDC). Thank you for the opportunity to testify today on CDC's vaccine safety research activities, particularly those regarding thimerosal-containing vaccines and autism. I want to take a moment to introduce Dr. Coleen Boyle, Associate Director for Science and Public Health with CDC's National Center for Birth Defects and Developmental Disabilities who is also available to help answer questions on CDC's autism-related activities.

CDC understands that autism can be a devastating illness that impacts families and caregivers alike. CDC joins with other federal and state agencies, and other partners in the continued search to learn more about the causes.

## **AUTISM AND VACCINES**

Autism spectrum disorders (ASD) are a group of life-long developmental disabilities caused by an abnormality of the brain. The most recent data suggests that between two and six children per 1,000 have ASD; however, one of CDC's goals is to obtain better information on the incidence and prevalence of ASDs. The emotional, social and economic impact on families of children diagnosed ASDs is often devastating and the costs to the nation in human and economic terms is substantial but needs to be better documented. We recognize that there is considerable public interest and concern on this issue and we are committed to addressing concerns of parents, families, caregivers and health care providers. The Department of Health and Human Services (DHHS) is dedicated to finding the answer to what causes autism and how it can be prevented. There is a great deal of ongoing research throughout the various public health agencies. While my focus today is on vaccine safety related issues, it should be noted that DHHS has established an Interagency Autism Coordinating Committee (IACC). The IACC is composed of representatives from the National Institutes of Health (to which the Department has delegated a leadership role in organizing and supporting the committee), CDC (including the Agency for Toxic Substances and Disease Registry (ATSDR)), the Food and Drug Administration, the Health Resources and Services Administration (HRSA) the Substance Abuse and Mental Health Services Administration (SAMHSA),

the Department of Education, and four public members appointed by Secretary Tommy Thompson. The IACC's mandate is to enhance coordination of the autism-related activities of these federal agencies, from biomedical research to services delivery. At the most recent IACC meeting, topics included the progress being made on implementation of autism research centers programs by NIH and CDC; efforts to comprehensively map the autism research field to analyze its strengths and any gaps; information about each of the individual grants that collectively constitute the majority of the NIH autism research portfolio; strategies to improve the coordination of gene and tissue banking, data sharing, and federal interactions with voluntary organizations; and, strategic planning for the development of treatments and interventions for autism. The activities of this committee highlight the large-scale, coordinated response that has been launched by DHHS to better understand, prevent and treat autism.

CDC also is holding four regional meetings to obtain more public input into the CDC portion of the IACC agenda; these meetings are being held over the next four months in Miami, FL; Sacramento, CA; Indianapolis, IN and in New York City.

Immunizations are one of the great public health success stories of the 20th century, having made once-common diseases, such as diphtheria, measles, mumps, and pertussis, diseases of the past. Vaccines are now available to protect children and adults against 15 life-threatening or debilitating diseases. This has reduced cases of all vaccine-preventable diseases by more than 97 percent from peak levels before vaccines were available, saving lives and saving treatment and hospitalization costs. However, some parents, researchers and others have expressed concerns about a potential link between autism and vaccines containing thimerosal, a preservative used to reduce the possibility of bacterial or fungal contamination of vaccines. Other than minor effects like swelling and redness at the injection site due to sensitivity to thimerosal, there is no definitive evidence of harm caused by the amounts of thimerosal in vaccines.

After an FDA analysis of the potential mercury content of the full recommended childhood vaccination services and concern about the health effects of mercury exposures

from all sources in mid-1999, the United States Public Health Service agencies, including NIH, FDA, HRSA, and CDC took precautionary action, working collaboratively with the American Academy of Pediatrics, the American Academy of Family Physicians and the vaccine manufacturers, to begin the voluntary removal of thimerosal preservative from the vaccine supply. While the risk of harm from exposure to thimerosal in vaccines was only theoretical, the decision was made as a precautionary measure. The elimination of mercury from vaccines was judged a feasible means of reducing an infant's total exposure to mercury in a world where other environmental sources of exposure are more difficult or impossible to eliminate, such as removal from certain foods and power emissions. As a result of this action, all manufacturers are now producing only vaccines that are free of thimerosal as a preservative for routine infant immunization, with the exception of influenza vaccine. As of January 14, 2003, the final lots of the routinely recommended childhood vaccines that contained thimerosal as a preservative, with the exception of influenza vaccine, expired.

### **CDC'S COMMITMENT TO VACCINE SAFETY**

CDC is actively involved in detecting and investigating vaccine safety concerns and supporting a wide range of vaccine safety research to address safety questions.

#### **Vaccine Safety Datalink Project**

CDC developed the Vaccine Safety Datalink (VSD) project in 1990 to better enhance the understanding of rare adverse effects of vaccines. This project is a collaborative effort, which utilizes the databases of eight large health maintenance organizations (HMOs). The database contains comprehensive medical and immunization histories of approximately 7.5 million children and adults. The VSD enables vaccine safety research studies comparing incidence of health problems between unvaccinated and vaccinated people. Over the past decade, the VSD has been used to answer many vaccine-related questions, and has been used to support policy changes that have reduced adverse effects from vaccines.

CDC recognizes the importance of data sharing when questions are raised regarding a particular study's design and methodology. Therefore, CDC worked with the participating HMOs to determine how their clients' personal medical records can be maintained confidentially and the proprietary interests of the HMOs protected, while still allowing for external researchers to reanalyze the data from studies which have been conducted through the Vaccine Safety Datalink. As a result, CDC has developed a data sharing process operated by the National Center for Health Statistics in collaboration with the National Immunization Program, which is designed to allow independent researchers to replicate or conduct a modified analysis of a previous VSD study, while maintaining the confidential and proprietary nature of the data.

### **Institute of Medicine Immunization Safety Review Committee**

Another critical part of our vaccine safety efforts is the objective, scientific evaluation of safety concerns by independent experts. In collaboration with NIH and other U.S. Public Health Service agencies, CDC requested the Institute of Medicine (IOM), one of the world's predominant medical organizations, to conduct independent reviews by objective, highly qualified scientific experts to determine: 1) whether the available scientific information tends to show, or does not tend to show, vaccines playing a role in causation; 2) the level of public health priority the concern should receive; and, 3) recommendations for research. The IOM Immunization Safety Review Committee has released reports on STET, Multiple Immunizations and Immune Dysfunction, and most recently Vaccines and Autism CDC has initiated a broad range of studies to address recommendations made by the IOM Immunization Safety Review Committee.

In October 2001, the IOM Immunization Safety Review Committee published a report on the possible association between thimerosal-containing vaccines and neurodevelopmental disorders. In this report, the IOM concluded "that the evidence is inadequate to accept or reject a causal relationship between exposure to thimerosal from childhood vaccines and the neurodevelopmental disorders of autism, ADHD (attention deficit hyperactivity disorder), and speech or language delay." The IOM made several recommendations regarding future research studies including several epidemiological studies. They recommended:

- Case-control studies examining the potential link between neurodevelopmental disorders and thimerosal-containing vaccines;
- Further analysis of neurodevelopmental outcomes in several cohorts of children outside the U.S. who participated in a clinical trial of DTaP vaccine; and,
- Conducting epidemiological studies that compare the incidence and prevalence of neurodevelopmental disorders before and after the removal of thimerosal from vaccines.

In May 2004, the IOM Immunization Safety Review Committee updated its conclusions and recommendations regarding vaccines and autism based on the additional studies that had been done on this topic since 2001. The IOM Immunization Safety Review Committee's most notable conclusions regarding thimerosal-containing vaccines were:

- thimerosal-containing vaccines are not associated with autism;
- hypotheses regarding a link between autism and thimerosal-containing vaccines lack supporting evidence and are only theoretical; and,
- future research to find the cause of autism should be directed toward other promising lines of inquiry that are supported by current knowledge and evidence and offer more promise for providing an answer.

The Committee also made a number of recommendations in the areas of policy, surveillance, and epidemiologic research, clinical studies, and communication in regard to thimerosal-containing vaccines, including:

- the Committee did not recommend a policy review of the current schedule and recommendations for the administration of routine childhood vaccines based on hypotheses regarding thimerosal and autism;
- the Committee recommended that cost-benefit assessments regarding the use of thimerosal-containing versus thimerosal-free vaccines and other biological or pharmaceutical products, whether in the United States or other countries, should not include autism as a potential risk; and,

- the Committee recommended developing programs to increase public participation in vaccine safety research and policy decisions and to enhance the skills and willingness of scientists and government officials to engage in constructive dialogue with the public about research findings and their implications for policy development.

The Committee has made helpful recommendations about policy and research in the areas of vaccine safety and autism. These will be considered in depth by the Public Health Service (PHS) agencies and their advisory bodies. At this time, CDC is making no changes to the current childhood immunization schedule and recommendations based on hypotheses regarding vaccines and autism.

### **Vaccine Safety Studies**

CDC takes the issue of vaccine safety very seriously and therefore undertook several studies that addressed the IOM recommendations from the 2001 report:

The first study, the Thimerosal Screening Analysis in the Vaccine Safety Datalink (VSD) project, was started in the fall of 1999. The VSD, described earlier, was used to screen for possible associations between exposure to thimerosal-containing vaccines and a variety of renal, neurologic and developmental problems. In the first phase of this study, the CDC used data from the 2 VSD HMOs with automated outpatient data (where more subtle effects of mercury toxicity might be seen). In phase I, an association between cumulative exposure to thimerosal and tics was found at one HMO. At the other HMO, slightly increased risks of language delay were found but there was no increased risk of tics. In the second phase of the investigation, CDC investigators examined data from a third HMO with similar available automated vaccination and outpatient databases to see if these findings could be replicated. Analyses of these data using the same methods as the first study did not confirm results seen in the first phase. I should note for the committee that it is not uncommon to find associations between health outcomes and an exposure of interest when multiple different health outcomes are assessed. To determine if those associations are real or occur by chance, the usual scientific approach is to

conduct other studies to confirm or not confirm the initial results. I also want to note that a statistically significant relationship between autism and thimerosal was not found in any of CDC's analysis of the VSD data. The findings from this study were published in the journal *Pediatrics* in November 2003.

CDC and VSD researchers remain committed to clarifying the results encountered during the VSD Screening Analysis; therefore, a Thimerosal and Neurodevelopmental Disorders (NDD) Follow-Up Study is being conducted. This second study will be designed to assess whether preliminary results from automated data used in the Thimerosal Screening Analysis can be confirmed using objective neuropsychological testing. The study will focus on the conditions found in the first screening analyses and other important neurodevelopmental disorders, including language and speech delays and ADHD. The design of the new study will address the main drawback of the Thimerosal Screening Analysis, which was that children were not objectively assessed on the neurodevelopmental disorders of interest. The various VSD HMOs categorize neurodevelopmental disabilities in different ways, provide different services for these disorders, and often refer children out of the health care network when they are identified with these particular disorders.

The Thimerosal and NDD Follow-Up Study will examine approximately 1,100 children between the ages of seven and nine years of age randomly selected from four VSD HMOs based on thimerosal exposure during the first seven months of life. All 1,100 children will be assessed using a standardized set of neuropsychological test batteries. The proposal for this study was presented to a panel of external consultants including a consumer representative in March of 2001. The panel of external consultants continues to provide individual input into the design and the conduct of the study. Data collection is nearing completion. The neuropsychological testing of the children has been completed and currently their medical records are being reviewed. The preliminary study results should be available for review by the external consultants by the spring of 2005.

Several additional studies are being planned to address additional issues raised by the IOM. These include:

The Vaccine Safety Datalink Thimerosal and Autism Study is a case-control study that will begin data collection this fall and will complement the Thimerosal and NDD Follow-Up Study. Autism cases identified through review of automated medical records from three VSD HMOs will be assessed objectively by using standardized autism assessment tools. Three controls per case will be selected from the same HMOs.

CDC is also funding a follow-up study of a group of Italian children who had participated in a prior DTaP trial in the 1990's in which thimerosal exposure was randomly allocated. A pilot study has determined the feasibility of recruiting these participants for a follow-up study of neurodevelopmental outcomes. The children will be evaluated using a similar test battery as in the Thimerosal and NDD Follow-Up Study. Testing of children for the main study will begin this fall.

Two other studies are being planned to examine changes over time in the diagnosis of neurodevelopmental delays including autism. These studies use inpatient and outpatient discharge diagnoses to compare rates of these conditions over time with changes in levels of thimerosal in recommended childhood vaccines. Because recommendations for the removal of thimerosal from vaccines did not occur until 1999, several years of data following the removal of thimerosal are necessary for these comparisons to be made. Thus, results will not be available until 2006 or later.

## **BENEFITS OF VACCINES**

While we remain vigilant to assure the safety of vaccines, we must also remember that vaccines benefit the public by protecting persons from infectious diseases and their consequences e.g. liver cancer. Continued high U.S. vaccination rates are crucial to prevent the spread of diseases such as measles, pertussis (whooping cough) and rubella among U.S. children. Current measles coverage is approximately 91 percent in children 19-35 months old and about 97 percent at school entry, and only about 100 cases of

measles have been reported per year; many of the cases are imported; and ongoing indigenous transmission of measles no longer occurs. From 1989-91, a measles epidemic in the United States led to more than 55,000 cases of measles and more than 11,000 hospitalizations, with 123 deaths in three years. Before this epidemic, vaccination coverage was estimated at 61-66 percent nationally and at 51-79 percent in 15 major cities. These outbreaks stopped only when vaccination coverage increased. Thus, if pre-school coverage dropped by 25-30 percent below the current level, large measles outbreaks are likely to occur once again. Additionally, pertussis has continued to be a public health threat. For example, in 2003, there were 11,647 reported pertussis cases with 19 reported deaths.

Vaccines are cited as one of the greatest achievements of biomedical science and public health in the 20th century. We can point to the remarkable success we have had in controlling numerous infectious diseases which used to be widely prevalent in the United States, including polio, measles, and pertussis. In fact, several of these vaccine-preventable infectious diseases are associated with developmental disabilities, including Haemophilus influenzae type b (Hib) and congenital rubella syndrome (CRS). Prior to routine immunization with Hib vaccine, of young children who developed Hib meningitis, 5 percent died and another 15 to 30 percent were left with residual brain damage leading to language disorders and mental retardation.

The threats posed by vaccine-preventable diseases are known and real. The viruses and bacteria that cause vaccine-preventable diseases still circulate in the U.S. and around the world. Maintaining vaccination coverage and high levels of immunity are crucial to protect the U.S. population and to continue progress toward elimination of diseases that, at one time, caused millions of infections in the U.S. each year and that globally remain the leading causes of death.

## **CONCLUSION**

CDC remains committed to collecting accurate data on the prevalence of autism, conducting public health research on autism, and conducting studies on vaccine safety. Vaccines are one of our most valuable weapons against disease and have afforded us one of our proudest achievements in public health. Autism research and monitoring will continue to be high priorities for CDC. Such efforts will be essential in answering key questions about whether autism is increasing over time, determining the cause(s) of this condition, and ultimately developing prevention strategies. In addition to these critical efforts, we also realize the need to act on existing science to improve the lives of children already living with this condition by promoting developmental screening and intervention. We want each child to be born healthy and to grow and develop to their full potential.

Thank you, Mr. Chairman and Members of the Committee, for the opportunity to testify before you today. Dr. Boyle and I would be happy to answer any questions that you may have.