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PREPARED STATEMENT ON INFLUENZA AND INFLUENZA VACCINE SAFETY AND  
SUPPLY

Chairman Regula and members of the subcommittee, I am pleased to be before you today to discuss the Centers for Disease Control and Prevention's (CDC) work and the important public health issues surrounding influenza and influenza vaccine safety. CDC is committed to the safety of the vaccine supply, as vaccines are essential tools for maintaining and improving the public's health. Vaccines offer protection from the threat of diseases, including influenza. Immunization plays a key role in lessening the impact of diseases, including influenza and is a core component of our efforts to prepare for this year's influenza season. In addition, immunization is at the center of the Department of Health and Human Services' strategy to prepare for an influenza pandemic.

#### **ROUTINE INFLUENZA VACCINATION RECOMMENDATIONS**

I have spoken to this Committee previously about the importance of vaccines in preventing disease, disability, and death, and I know that you all agree that vaccines are a vital tool for protecting the public's health. In particular, influenza is a serious disease resulting in approximately 36,000 deaths and 200,000 hospitalizations in the United States each year. Although the majority of influenza deaths occur among the elderly, during the 2003-2004 influenza season, there were 153 influenza-related deaths among children under the age of 18 reported to CDC. Because recent studies have demonstrated high rates of hospitalization of young children, the Advisory Committee on Immunization Practices (ACIP) has expanded its vaccination recommendations to recommend that all children between the ages of 6 months and 23 months as well as all children 6 months or older with certain risk factors receive the influenza vaccine. The ACIP made this recommendation, noting that, "The risks of severe illness from

influenza infection are elevated among both young children and pregnant women, and both groups benefit from vaccination by preventing illness and death from influenza.”

### **PREVENTING DISEASE, DISABILITY, AND DEATH THROUGH VACCINATION**

Moreover, 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 in the United States and other developed countries. Vaccines are now available to protect children and adults against 15 life-threatening or debilitating diseases. Through our immunization efforts, we have reduced cases of vaccine-preventable diseases in the U.S. by more than 97 percent from peak levels before vaccines were available. This saves lives as well as treatment and hospitalization costs. Vaccines benefit both the individual who receives the vaccine as well as the community at large, and continued high vaccination rates in the United States are crucial to prevent the spread of diseases such as measles, pertussis and rubella and other diseases that, at one time, caused millions of infections in the United States each year and that today remain globally among the leading causes of death.

#### ***Removal of Thimerosal from Routinely Recommended Infant Vaccines***

Vaccines prevent death and disease, and they contribute to reductions in healthcare costs. However, some have expressed concerns about the safety of vaccines, particularly those containing thimerosal, an ethyl mercury containing preservative that has been used to prevent bacterial or fungal contamination of the product for over 50 years. Before vaccines are released by the FDA they are assessed for sterility. However, vaccines packaged in multidose vials contain a preservative to eliminate the risk that bacteria or fungus could be inadvertently introduced into the vial by health care

professional when they insert the needle through the stopper to withdraw a dose. 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.

Despite this, in mid-1999, the United States Public Health Service Agencies, including the Food and Drug Administration (FDA), National Institutes of Health (NIH), CDC, and the Health Resources and Services Administration (HRSA) 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. This action was taken following an FDA analysis of the potential mercury content of the full recommended childhood vaccination schedule and in response to public concerns about the health effects of mercury exposure from all sources. In this review, it was recognized that depending on which vaccines a child received, it was possible that some children could be exposed to a cumulative level of ethyl mercury over the first six months of life that exceeded one of the federal guidelines on methyl mercury. Although there is no evidence that thimerosal in vaccines is health risk to the general public, the elimination of ethyl 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 of vaccine used in the U.S. are

now producing only vaccines that are free of thimerosal as a preservative for routine infant immunization, with the exception of influenza vaccine. In practical terms, to a large degree this shift in policy resulted in a shift away from multidose vials to single dose preparations. 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. However, thimerosal-preservative-free influenza vaccine is available and licensed for use in children 6 months and older.

#### **INSTITUTE OF MEDICINE IMMUNIZATION SAFETY REVIEW COMMITTEE**

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.

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 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. In its most recent statement on influenza vaccines (May 28, 2004), the ACIP, an external expert advisory committee to the CDC Director and the Secretary of Health and Human Services, said, “The risks of severe illness from influenza infection are elevated among both young children and pregnant women, and both groups benefit from vaccination by preventing illness and death from influenza. In contrast, no scientifically conclusive evidence exists of harm from exposure to thimerosal preservative-containing vaccine, whereas evidence is accumulating of lack of any harm resulting from exposure to such vaccines. Therefore, the benefits of influenza vaccination outweigh the theoretical risk, if any, for thimerosal exposure through vaccination. Nonetheless, certain persons remain concerned

regarding exposure to thimerosal. The U.S. vaccine supply for infants and pregnant women is in a period of transition during which thimerosal in vaccines intended for these groups is being reduced by manufacturers as a feasible means of reducing an infant's total exposure to mercury because other environmental sources of exposure are more difficult or impossible to eliminate. Reductions in thimerosal in other vaccines have been achieved already and have resulted in substantially lowered cumulative exposure to thimerosal from vaccination among infants and children. For all of these reasons, persons recommended to receive inactivated influenza vaccine may receive either vaccine preparation, depending on availability.”

Nonetheless, the National Vaccine Program Office (NVPO) in the Department of Health and Human Services is working with CDC and FDA to coordinate an orderly transition to an expanded supply of thimerosal preservative-free influenza vaccine without disrupting production and distribution of influenza vaccine to those who are at greatest risk of suffering severe illness or death. This coordinated effort involves the American Academy of Pediatrics, the American Academy of Family Physicians, the American Academy of Pediatrics, the American Medical Association and the American College of Physicians as well as the influenza vaccine manufacturers. Together, this group is working to protect Americans from influenza by maintaining sufficient vaccine supplies while developing plans to reduce the use of thimerosal preservative.

However, it is important to accomplish a transition to thimerosal preservative-free influenza vaccine in an orderly and thoughtful way. Most currently available influenza vaccine is packaged in multi-dose vials. FDA regulations require preservatives in multi-dose vials of most vaccines, including multi-dose influenza

vaccine preparations, to protect against inadvertent contamination from repeated puncture of the vial's seal. Current production capacity for thimerosal-free influenza vaccine falls far short of the need. Of the approximately 100 million doses of influenza vaccine that will be produced for the 2004-2005 influenza season, we estimate 4.6 million will be single-dose thimerosal-preserved-free preparations licensed for use in children (including 500,000 late production doses that are expected in December and January 2005). We estimate that 11.9 million doses would be needed just to meet the new recommendation to immunize children ages 6 months to 23 months. (Based upon census estimates, the size of this group is approximately 6.1 million children. Assuming that 95% of these children will require 2 doses of vaccine and 5% will require 1 dose of vaccine, the total number of doses needed is 11.9 million).

Over the next several years, the only manufacturer of influenza vaccine for children under 4 years of age estimates it will have the capacity to produce each year about 8 million doses of thimerosal-free vaccine. Building new capacity takes financial investments and time, and at this time, we are unable to estimate when the supplies of thimerosal-preserved-free vaccine will be available for all children.

### ***Pandemic Influenza Planning and Preparedness***

This issue is particularly relevant in light of the Department's pandemic influenza planning and preparedness efforts. Today, many influenza experts, including those at CDC, consider the threat of a serious influenza pandemic to the United States to be high. Although the timing and impact of an influenza pandemic is unpredictable, the occurrence is inevitable and potentially devastating.

To prepare for this event, the Department of Health and Human Services released the draft Pandemic Influenza Response and Preparedness Plan in August 2004. The plan addresses the roles of federal, state, and local agencies in a pandemic response; identifies vaccination as the primary strategy to reduce the health impact of a pandemic; and recognizes and prepares for the challenges and barriers to adequate domestic production of vaccine in the event of an influenza pandemic.

A pandemic – or global epidemic – occurs when there is a major change in the influenza virus so that most or all of the world’s population has had no previous exposure and is therefore vulnerable to the virus. Three influenza pandemics occurred during the 20th century. The most recent influenza pandemic which occurred in 1968, commonly referred to as “Hong Kong” Influenza, resulted in nearly 34,000 deaths in the United States. In 1957, the “Asian” flu pandemic resulted in about 70,000 deaths, and the most deadly influenza pandemic was the 1918 Spanish influenza pandemic, which caused 20 million deaths worldwide. Between September 1918 and April 1919, approximately 675,000 deaths from the Spanish influenza pandemic occurred in the United States alone. Recent outbreaks of human disease caused by avian influenza strains in Asia, Europe, and North America and the news from the World Health Organization last week that there is now evidence of limited person-to-person transmission of this avian (H5N1) virus in rural Thailand, highlight the potential for the introduction and spread of new strains of the influenza virus in the human population. Studies suggest that avian strains have become endemic in some wild birds and that these strains are becoming more capable of causing severe disease in humans. If this virus develops an ability to be efficiently transmitted from person-to-person, a severe

pandemic could occur. An influenza pandemic has a greater potential to cause rapid increases in death and illness than virtually any other natural health threat, and should an influenza pandemic occur, vaccination will play a key role in protecting the American public. Yet, given our current influenza vaccine manufacturing technology, the production of pandemic influenza vaccine will take several months, and in such an emergency, it will be critical that the production of this vaccine be provided in multi-dose vials, which for safety reasons will require the use of preservative, to ensure that as many Americans as possible are protected as soon as possible.

Therefore, any premature requirement, not based on sound science or current manufacturing capacity, to remove thimerosal preservative from influenza vaccines would have severe repercussions on influenza vaccine supply and our preparedness against yearly influenza outbreaks as well as the threat of pandemic influenza.

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

Recognizing that immunization is one of the most effective public health interventions and that it is an important tool in to protect the public's health, CDC takes very seriously concerns regarding the safety of vaccines. Therefore, CDC remains actively involved in monitoring vaccine safety and supporting a wide range of research to address safety questions.

#### ***Vaccine Adverse Event Reporting System***

CDC and FDA maintain the national Vaccine Adverse Event Reporting System (VAERS), which monitors adverse events following immunization. Since 1990, VAERS has received over 128,000 reports, most of which describe mild side effects such as fever. However, the system has captured rare, more serious adverse events

following immunization. VAERS helps to identify safety concerns so that we can take action to further promote and protect the nation's health. CDC is working to encourage further use of VAERS by physicians and other health care professionals to report adverse events and has recently implemented a web-based interface so that the full potential of this tool can be realized.

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

In 1990, CDC developed the Vaccine Safety Datalink (VSD) to better enhance the understanding of rare adverse effects of vaccines. In collaboration with several large managed care organizations (MCOs) the VSD provides a large database that includes comprehensive medical histories, including the immunization records of approximately 7.5 million children and adults. The VSD allows researchers to compare health events of unvaccinated and vaccinated people. CDC has implemented a data sharing process to allow independent researchers the opportunity to conduct new studies as well as reanalyze datasets of published VSD studies. Recently, in an effort to improve public access without compromising patient confidentiality, the management of this activity was relocated from the National Immunization Program to CDC's National Center for Health Statistics in Hyattsville, Maryland.

### **CDC'S AUTISM ACTIVITIES**

I have listened to families affected by autism, and I understand the concerns of these families who are seeking answers about what caused their sons and daughters to develop an autism spectrum disorder (ASD). I recognize that there are unanswered questions about what causes these disorders, and 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 influenza and 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, the Agency for Toxic Substances and Disease Registry, FDA, HRSA, the Substance Abuse and Mental Health Services Administration, 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.

## **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. 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. We live in a global community and 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 as the leading causes of death.

#### **CONCLUSION**

In conclusion, I would like to thank you for your time and for bringing attention to these important public health issues. CDC is committed to protecting and promoting health for all Americans and preventing disease and disability through public health research and public outreach and support of important interventions including vaccination. Recognizing the important role of vaccines in protecting the health of all Americans and for preparing for future threats, we will continue to ensure the highest possible level of vaccine supply safety through ongoing safety monitoring and research. In addition, although the available research does not support a relationship between vaccines and autism, DHHS will continue working with industry to increase production of thimerosal-preservative-free vaccines. Finally we will continue searching for other causes, and work to support programs designed to lessen the impact of autism spectrum disorders on affected families. Thank you for your interest in this issue and your support of CDC's immunization programs.