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CHILDHOOD VACCINES

Challenges in Preventing
Future Shortages

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Mr. Chairman and Members of the Subcommittee:

We are pleased to be here today to discuss recent childhood vaccine shortages. Today we are releasing our report that you, along with seven other Members of the Congress, requested on the subject.¹ My statement today highlights some of the key aspects of our report.

The recent incidents of vaccine shortages began in November 2000 when supplies of the tetanus and diphtheria booster (Td) fell short. By October 2001, the Centers for Disease Control and Prevention (CDC) reported shortages of five vaccines that, because some are combination vaccines, protect against eight childhood diseases. In addition to diphtheria and tetanus vaccines, vaccines to protect against pertussis, invasive pneumococcal disease, measles, mumps, rubella, and varicella were in short supply. In July 2002, updated CDC data indicated supplies were returning to normal for most vaccines. However, the shortage of vaccine to protect against invasive pneumococcal disease was expected to continue through at least late 2002. Concerned about the impact of and reasons for these shortages, you asked that we examine the following questions:

1. To what extent have recent childhood vaccine shortages affected immunization policies and programs?
2. What factors have contributed to the recent shortages, and have they been resolved?
3. What strategies are federal agencies considering to help mitigate disruptions in the vaccine supply?

In brief, shortages have prompted federal authorities to recommend deferring some vaccinations and have caused the majority of states to reduce or suspend immunization requirements for school and day care programs so that children who had received fewer than the previously mandatory immunizations could enroll. States are concerned that failure to be vaccinated at a later date may reduce the share of the population protected and increase the potential for disease to spread; however, data are not currently available to measure these effects.

¹U.S. General Accounting Office, *Childhood Vaccines: Ensuring an Adequate Supply Poses Continuing Challenges*, [GAO-02-987](#) (Washington, D.C.: Sept. 13, 2002).

Multiple factors, including production problems and unanticipated demand for newly approved vaccines, contributed to recent vaccine shortages. While problems leading to the shortages have largely been resolved, the potential exists for shortages to recur. The complex nature and often year-long production schedule of manufacturing a vaccine will continue to make it difficult for the supply system to respond rapidly to sudden changes in supply or demand. Additionally, so few firms make each vaccine (five of the eight recommended childhood vaccines have only one manufacturer each), that production problems or a manufacturer's decision to withdraw may leave few or no alternative sources of vaccine. One development that may increase the supply of vaccines is that a number of new vaccine products that could be used to meet the existing childhood immunization schedule are in varying stages of development. However, completing clinical testing and review by the Food and Drug Administration (FDA) will likely take several years, as these products generally do not qualify for expedited review under FDA policies.

Federal agencies and advisory committees are exploring options to help stabilize the nation's vaccine supply, but few long-term solutions have emerged. Approaches under consideration include strengthening manufacturers' protection against liability for injuries related to childhood vaccines and streamlining the regulatory process. While CDC is considering expanding vaccine stockpiles to provide a cushion in the event of a supply disruption, limited supply and manufacturing capacity will restrict CDC's ability to build them. CDC also lacks a strategy for determining such things as how much vaccine to stockpile, where it should be stored, and how to ensure that the stockpile is additional to a manufacturer's normal inventory. In addition, it is unclear whether the authority that CDC is using to establish these stockpiles provides for their use for all children.

Background

Immunizations are widely considered one of the leading public health achievements of the 20th century. Mandatory immunization programs have eradicated polio and smallpox in the United States and reduced the number of deaths from several childhood diseases, such as measles, to near zero. A consistent supply of many different vaccines is needed to support this effort. CDC currently recommends routine immunizations against 11 childhood diseases: diphtheria, tetanus, pertussis (whooping

cough), *Haemophilus influenzae* type b (most commonly meningitis), hepatitis B, measles, mumps, rubella (German measles), invasive pneumococcal disease, polio, and varicella (chicken pox).² By combining antigens (the component of a vaccine that triggers an immune response), a single injection of a combination vaccine can protect against multiple diseases.

The federal government, primarily through agencies of the Department of Health and Human Services (HHS), has a role both as a purchaser of vaccines and as a regulator of the industry. The federal government is the largest purchaser of vaccines in the country. CDC negotiates large purchase contracts with manufacturers and makes the vaccines available to public immunization programs under the Vaccines for Children (VFC) program. Under VFC, vaccines are provided for certain children, including those who are eligible for Medicaid or uninsured. Participating public and private health care providers obtain vaccines through VFC at no charge. A second program, established under section 317, of the Public Health Service Act, provides project grants for preventive health services, including immunizations. Currently, CDC supports 64 state, local, and territorial immunization programs (for simplicity, we refer to them as state immunization programs). In total, about 50 percent of all the childhood vaccines administered in the United States each year are obtained by public immunization programs through CDC contracts.

The federal government is also responsible for ensuring the safety of the nation's vaccine supply. FDA regulates the production of vaccines. It licenses all vaccines sold in the United States, requiring clinical trials to demonstrate that vaccines are safe and effective, and reviews the manufacturing process to ensure that vaccines are made consistently in compliance with current good manufacturing practices. Once vaccines are licensed, FDA also conducts periodic inspections of production facilities to ensure that manufacturers maintain compliance with FDA manufacturing requirements.

States also have an important role in immunization efforts. Policies for immunization requirements, including minimum school and day care entry requirements are made almost exclusively at the state level, although cities

²The CDC recommended immunization schedule combines the recommendations approved by the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians.

occasionally impose additional requirements. Each state also established an immunization infrastructure to monitor infectious disease outbreaks, administer federal immunization grants, manage centralized supplies of vaccine, and otherwise promote immunization policies.

Shortages Prompt Actions to Reduce Immunization Requirements

Recent vaccine shortages have necessitated temporary modifications to the recommended immunization schedule and have caused states to scale back immunization requirements. In our survey of 64 state immunization programs, administered through the Association for State and Territorial Health Officials (ASTHO), all 52 responding programs indicated that they had experienced shortages of two or more vaccines and had taken some form of action to deal with the shortages. Vaccine shortages experienced at the state level have, in turn, prompted cutbacks in immunization requirements for admission to day care or school. Thirty-five states reported putting into effect new, less stringent immunization requirements that allow children who have received fewer than the recommended number of vaccinations to attend school. In general, these states have reduced the immunization requirements for day care and/or school entry or have temporarily suspended enforcement of those requirements until vaccine supplies are replenished. For example, the Minnesota Department of Health suspended the school and postsecondary immunization laws for Td vaccine for the second year in a row, with the suspension extending through the 2002-2003 school year. Other states, including South Carolina and Washington, reported allowing children to attend day care or school even if they were not in compliance with immunization requirements, under the condition that they be recalled for vaccinations when supplies became available.

While it is too early to measure the effect of deferred vaccinations on immunization rates, a number of states reported that vaccine shortages and missed make-up vaccinations may take a toll on coverage and, therefore, increase the potential for infectious disease outbreaks. The full impact of vaccine shortages is difficult to measure for several reasons. For example, none of the national immunization coverage surveys measures vaccination coverage of children under the age of 18 months—the age

cohort receiving the majority of vaccinations.³ While immunization experts generally agree that the residual effects of historically high immunization rates afford temporary protection for underimmunized children, missed immunizations could make susceptible children vulnerable to disease outbreaks. For example, a CDC analysis of a 1998 outbreak of measles in an Anchorage, Alaska, school showed that only 51 percent of the 2,186 children exposed had received the requisite two doses of measles vaccine.

Problems Causing Shortages Largely Resolved, but Shortages Could Recur

No single reason explains the rash of recent vaccine shortages; rather, multiple factors coincided that affected both the supply of and demand for vaccines. We identified four key factors, as follows.

Production Problems - Manufacturing production problems contributed to the shortage of certain vaccines. In some cases, production slowdowns or interruptions occurred when planned maintenance activities took longer than expected; in other cases, production was affected as manufacturers addressed problems identified in FDA inspections. Changes over the last several years in FDA inspection practices may have resulted in the identification of more or different instances of manufacturers' noncompliance with FDA manufacturing requirements. For example, prior to these changes, biologics inspections tended to focus primarily on scientific or technical issues and less on compliance with good manufacturing practices and documentation issues. FDA did take some steps to inform manufacturers about its inspection program changes; however, some manufacturers reported problems related to how well the changes were communicated. FDA issued a compliance program guidance manual detailing the new protocol for conducting inspections intended for FDA staff. However, the information in it could have provided manufacturers a better understanding of the scope of the inspections, but the manual was not made widely available—only upon request.

Removal of Thimerosal - Calls for the removal of the preservative thimerosal from childhood vaccines illustrate the effect that policy changes can have on the supply of vaccine. As a precautionary measure, in

³In August 2002, CDC reported that a limited study in Puerto Rico found a marked decrease in DTaP coverage consistent with CDC's recommendation to defer the fourth dose of DTaP. See Centers for Disease Control and Prevention, "Impact of Vaccine Shortage on Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Coverage Rates Among Children Aged 24 Months-Puerto Rico, 2002," *Morbidity and Mortality Weekly Report*, vol. 51, no.30 (2002): 667-668.

July 1999, the American Academy of Pediatrics (AAP) and the U.S. Public Health Service (PHS) issued a joint statement advising that thimerosal in vaccines be eliminated or reduced as soon as possible.⁴ While thimerosal was present in several vaccines, removing it from some vaccines was more complex than for others. For example, one manufacturer of the diphtheria-tetanus-acellular pertussis vaccine (DTaP) had to switch its packaging from multidose to single-dose vials due to the removal of the preservative. This process reduced the manufacturer's output of vaccine by 25 percent, according to the manufacturer.

Manufacturer's Decision to Discontinue Production - Another major factor in the shortage of DTaP, and also Td, was the decision of one manufacturer to discontinue production of all products containing tetanus toxoid. With little advance warning, the company announced in January 2001 that it had ceased production of these vaccines. According to the manufacturer, prior to its decision, it produced approximately one-quarter of all Td and 25 to 30 percent of all DTaP distributed in the United States, so the company's departure from these markets was significant. In the previous year, another manufacturer that supplied a relatively small portion of DTaP also had stopped producing this vaccine. Together these decisions decreased the number of major manufacturers of DTaP from four to two and of Td from two to one.⁵

Unanticipated Demand - The addition of new vaccines to the recommended immunization schedule can also result in shortages if the demand for vaccine outstrips the predicted need and production levels. This was the case with a newly licensed vaccine, pneumococcal conjugate vaccine (PCV), which protects against invasive pneumococcal diseases in young children. PCV was licensed by FDA in February 2000 and formally added to the recommended schedule in January 2001. Company officials said an extensive education campaign prior to its availability resulted in record-breaking initial demand for the vaccine. CDC reported shortages of PCV existed through most of 2001, and the manufacturer was only able to provide about half the needed doses during the first 5 months of 2002.

⁴The joint statement by AAP and PHS also stated that the large risk of not vaccinating children far outweighs the unknown and probably much smaller risk, if any, of cumulative exposure to thimerosal-containing vaccines in the first 6 months of life.

⁵In addition to the one major nationwide supplier of Td, a second manufacturer produces a small amount of Td, primarily for local distribution, and makes some available for nationwide distribution.

Ongoing manufacturing problems limit production, exacerbating the shortage.

While the recent shortages have been largely resolved, the vaccine supply remains vulnerable to any number of disruptions that could occur in the future—including those that contributed to recent shortages and other potential problems, such as a catastrophic plant fire. One key reason is that the nature of vaccine manufacturing prevents the quick production of more vaccine when disruptions occur. Manufacturing a vaccine is a complex, highly controlled process, involving living biological organisms, that can take several months to over a year. Another underlying problem is the limited number of manufacturers—five of the eight recommended childhood vaccines have only one major manufacturer each. Consequently, if there are interruptions in supply or if a manufacturer ceases production, there may be few or no alternative sources of vaccine.

One situation that may help add to the supply of existing vaccines is the development of new vaccines. A recent example is a new formulation of DTaP that recently received FDA approval and has helped ease the shortage of DTaP. We identified 11 vaccines in development that could help meet the current recommended immunization schedule. These vaccines, some of which are already licensed for use in other countries, are in various stages of development, but all must undergo a rather lengthy process of clinical testing and FDA review. While FDA has mechanisms available to shorten the review process, they are not used for most vaccines under development. FDA policies generally restrict the use of its expedited review processes to vaccines that offer protection against diseases for which there are no existing vaccines. Because childhood vaccines under development often involve new forms or combinations of existing vaccines, they typically do not qualify for expedited FDA review.

No Clear Path Yet to Resolve Ongoing Supply Issues

Federal efforts to strengthen the nation's vaccine supply have taken on greater urgency with the recent incidents of shortages. As part of its mandate to study and recommend ways to encourage the availability of safe and effective vaccines, the National Vaccine Advisory Committee formed a work group to explore the issues surrounding vaccine shortages and identify strategies for further consideration by HHS. In its preliminary report, the work group identified several strategies that hold promise, such as streamlining the regulatory process, providing financial incentives for vaccine development, and strengthening manufacturers' liability protection, but it concluded that these strategies needed further study. The work group did express support for expanding CDC vaccine stockpiles

In response to the work group's finding that streamlining the regulatory process needed further study, FDA recently announced that it is examining regulations governing manufacturing processes for both drugs and vaccine products to determine if reform is needed. However, FDA officials told us it is too early to define the scope and time frame for this reexamination. Regarding financial incentives for vaccine development, the Institute of Medicine is currently conducting a study of vaccine pricing and financing strategies that may address this issue.

In regard to liability protections, the work group did make recommendations to strengthen the Vaccine Injury Compensation Program (VICP). VICP is a federal program authorized in 1986 to reduce vaccine manufacturers' liability by compensating individuals for childhood-vaccine-related injuries from a VICP trust fund. The program was established, in part, to help stem the exodus of manufacturers from the vaccine business due to liability concerns. Manufacturers, however, reported a recent resurgence of childhood-vaccine-related lawsuits—including class action lawsuits related to past use of thimerosal—that allege that the lawsuits are not subject to VICP. While the work group acknowledged that recent vaccine shortages do not appear to be related to VICP liability issues, it indicated that strengthening VICP would encourage manufacturers to enter, or remain in, the vaccine production business. Legislation has been introduced for the purpose of clarifying and modifying VICP.⁶

Expansion of Stockpiles Is under Consideration

Also consistent with the work group's recommendations, CDC is considering whether additional vaccine stockpiles will help stabilize the nation's vaccine supply. In 1993, with the establishment of the VFC program, CDC was required to purchase sufficient quantities of pediatric vaccines not only to meet normal usage, but also to provide an additional 6-month supply to meet unanticipated needs. Further, to ensure funding, CDC was authorized to make such purchases in advance of appropriations. Despite this requirement, to date, CDC has established partial stockpiles for only two—measles-mumps-rubella (MMR) and inactivated polio vaccine (IPV)—of the eight recommended childhood vaccines.

⁶See S. 2053, H.R. 1287, and H.R. 3741.

Even if CDC decides to stockpile additional vaccines, the limited supply and manufacturing capacity will restrict CDC's ability to build certain stockpiles in the near term. CDC estimates it could take 4 to 5 years to build stockpiles for all the currently recommended childhood vaccines—at a cost of \$705 million. Past experience also demonstrates the difficulty of rapidly building stockpiles. Neither the current IPV nor MMR stockpiles have ever achieved target levels because of limited manufacturing capacity. In addition to these challenges, CDC will also need to address issues regarding its authority, strategy, and information needed to use stockpiled vaccines.

Authority - It is uncertain whether stockpiled vaccines purchased with VFC funds can be used for non-VFC-eligible children. While the 1993 legislation required the Secretary of HHS to negotiate for a 6-month stockpile of vaccines to meet unanticipated needs, the legislation did not state that the supply of stockpiled vaccines may be made available for children not otherwise eligible through the VFC program. CDC officials said that the VFC legislation is unclear as to whether stockpiled vaccines can be used for all children.

Strategy - Expanding the number of CDC vaccine stockpiles will require a substantial planning effort—an effort that is not yet complete. For example, CDC has not made key decisions about vaccine stockpiles to ensure their ready release, including the quantity of each vaccine to stockpile, the form of storage, and storage locations. Also, to ensure that use of a stockpile does not disrupt supply to other purchasers, procedures would need to be developed to ensure that stockpiles represent additional quantities to a manufacturer's normal inventory levels.

Information - Once sufficient quantities of vaccines are stockpiled in the appropriate form, CDC needs to make wise decisions on when to deploy the stockpiles. However, CDC currently lacks information for effective decisionmaking. Releasing vaccine from a stockpile in a timely manner requires accurate prediction of a number of variables related to the early identification, severity, and duration of the supply disruption. CDC currently has data that it uses to screen for disruptions in vaccine supply to state immunization programs, but does not have data to anticipate a supply disruption or to fully evaluate the potential severity and duration of a supply disruption, especially to private providers. Through its facility inspections and approvals of production lots, FDA has important information about manufacturers' levels of vaccine production and plant conditions that could affect production. This information could help CDC anticipate supply disruptions and independently assess their potential

severity, but it is only available to CDC by written request. With such information, CDC could set priorities for or resize states' orders and determine how much stockpiled vaccine to release and when to release it. Timely information is important because releasing vaccine from a stockpile can take up to 30 days.

Concluding Observations

The vaccine shortages experienced over the last 2 years demonstrate the vulnerability of the vaccine supply to disruption. Federal agencies are continually challenged to take a proactive approach within their existing missions to help mitigate the effects of these potential future disruptions. Accordingly, our report makes several recommendations to the Secretary of HHS to help promote the availability of vaccine products. These recommendations include adding vaccines to the types of products that can be considered under FDA authority to expedite approval of products in development and directing CDC to address several operational and strategic issues in expanding childhood vaccine stockpiles. The report also contains a matter for congressional consideration to amend the VFC program legislation to address whether vaccines stockpiled under the program are available for use by all children in the event of a shortage.

This concludes my prepared statement, Mr. Chairman. I will be happy to respond to any questions that you or Members of the Subcommittee may have.

Contacts and Acknowledgments

For future contacts regarding this testimony, please call Janet Heinrich, Director, Health Care—Public Health Issues, at (202) 512-7119 or Frank Pasquier at (206) 287-4861. Other individuals who made key contributions include Jennifer Major, Linda McIver, Terry Saiki, and Leslie Spangler.