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PROTECTING OUR KIDS: WHAT IS CAUSING THE CURRENT SHORTAGE IN CHILDHOOD VACCINES?

HEARING

BEFORE THE

COMMITTEE ON
GOVERNMENTAL AFFAIRS
UNITED STATES SENATE

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WEDNESDAY, JUNE 12, 2002

U.S. SENATE,
COMMITTEE ON GOVERNMENTAL AFFAIRS,
Washington, DC.

The Committee met, pursuant to notice, at 9:37 a.m., in room SD–342, Dirksen Senate Office Building, Hon. Joseph I. Lieberman, Chairman of the Committee, presiding.

Present: Senators Lieberman, Carnahan, and Bunning.

OPENING STATEMENT OF CHAIRMAN LIEBERMAN

Chairman LIEBERMAN. Good morning. I apologize for being breathless. I did my walk up the stairs to beat the slow elevator. I apologize for being late, Washington traffic.

I want to thank all of you for coming to this hearing on this very disturbing subject of the shortage of childhood vaccines. The truth is, what could be worth more of our time and energy than trying to figure out how to fully protect the smallest among us—the children who are so innocent—from disease and from death?

This is a topic that could easily be overlooked in the rush of what seem to be more critical stories these days, and the fact that this Committee has not overlooked it is solely the work of our colleague, Senator Jean Carnahan, whose longstanding commitment to children's health issues is perhaps not as well known as it should be, but certainly most admirable. Today's hearing was her idea. I thank her for focusing this Committee's attention on this area. I want to say a few words in introduction and then I am happy to turn the gavel over to Senator Carnahan to conduct the hearing. I also thank Senator Bunning for the interest that he shows by being here, as well.

In this medically advanced world we live in, it is all too easy to forget the real value of traditional vaccines, that is to say, when we are so focused on miracle cures, etc. Many of today's parents, and it pains me to say this, are too young to remember what some of us who are just a bit older remember, and that is the awful days when diseases such as polio or measles were incurable.

In 1900—I was not alive then, I want to make the record clear on that—— [Laughter.]

It is just a statistically significant date. Twelve out of every 100 infants died from preventable diseases. Today, the number of chil-

dren afflicted by these illnesses has fallen by more than 99 percent. The reason, of course, is the invention of the modern vaccine.

The overwhelmingly successful public health campaign to innoculate all children against disease is a story of cooperation between public health agencies, scientists, government, and hundreds of thousands of local health care providers. In 1993, President Clinton extended the success story to include uninsured and under-insured children through the Vaccine for Children program.

But there is a danger now which this hearing will highlight, and I know Senator Carnahan is very concerned about, that we are slipping backwards. Just as we have reached vaccination rates that are quite high, we now face alarming shortages of these priceless serums. In the last 2 years, we have seen shortfalls in the supply of five of the eight vaccines that fight the major childhood illnesses. Some school systems have even been forced to adjust their mandatory vaccination schedules because of inadequate supply.

So our task today is to examine the scientific, financial, and practical obstacles to maintaining an adequate and safe supply of vaccines. But in the richest, most powerful Nation in the history of the world, there really is not an acceptable excuse that can justify immunizing fewer children today than we did 5 years ago.

This is a very distinguished group of witnesses that Senator Carnahan has assembled. I urge them to be frank in telling the Committee what we can do to help you do your job, because this really is a labor of love. Clearly, we have got to continue to uphold high standards in approving new vaccines and monitoring the production of the more established ones, and we have got to ensure that the Vaccine Injury Compensation Fund cares for those affected by the rare complications of vaccinations.

Dr. Jonas Salk, in administering the experimental polio vaccine to himself, his wife, and three sons in 1955 said, "It is courage based on confidence, not daring, and it is confidence based on experience." I think we have got to show a similar courage, for experience has clearly informed us of the value of vaccines.

Again, I thank Senator Carnahan for her extraordinary leadership here. I thank Senator Bunning for being a partner in that leadership, and I am happy now to turn the gavel over to you, Senator Carnahan. Thank you.

OPENING STATEMENT OF SENATOR CARNAHAN

Senator CARNAHAN [presiding]. Thank you, Senator Lieberman. Thank you for being here today and for permitting me the opportunity to hopefully shed some light on this very, very important subject.

Chairman LIEBERMAN. I am sure you will.

Senator CARNAHAN. Thank you. I am going to make an opening statement at this time, and then Senator Bunning will make an opening statement, and then we will turn to our witnesses who are with us today.

I would like to read you something. "To Our Patients: Recently, all pediatric practices nationwide have been experiencing shortages of required immunizations. It was not until the first week of December 2001 that this shortage directly affected our patients at Northwest Pediatrics. Despite a great effort on our part, we have

been unable to obtain some of the vaccines recommended and required. It has become necessary to alter the present immunization schedule. A phone log will be kept to inform you as soon as adequate supplies become available. Please address specific questions to your provider. Thank you for your understanding."

Well, this notice is dated December 2001. It is now June 2002 and the sign continues to hang in the examining room of the Northwest Pediatric Clinic in St. Louis, Missouri. To not have these basic vaccines available for our children is a national disgrace. Unfortunately, it is a sad reality for both private and public health facilities throughout Missouri and across the Nation.

For over a year, routine childhood vaccines have been in short supply. The precise impact depends on the specific community and what day you talk to them. In late May, public and private health providers in Springfield, Missouri, were experiencing a shortage in pneumoccal, which protects against meningitis and pneumonia; varicella, which protects against chicken pox; and the tetanus booster shot for adolescents.

The Cole County Public Health Department in Central Missouri was experiencing a shortage in DTaP, and MMR, as well as varicella and tetanus.

And when my office spoke to a pediatrician in Poplar Bluff, Missouri, her practice happened to be having a good week where no vaccine was in short supply. However, the medical staff we spoke to said that next week could, once again, bring a shortage.

The current supply crisis, if it continues, would lead to a giant step backwards in public health in this country. Young parents have not seen these terrible diseases that vaccines prevent. They do not remember polio or whooping cough because vaccines have accomplished their mission.

I can tell you that I remember these diseases. I know from personal experience the value of vaccines, and we do not want to move backwards. When I was a young girl, the vaccine for whooping cough was developed. This was a new vaccine and my mother was afraid to give it to me. At 4 years old, I developed the disease, and I can still remember that awful experience.

I also remember what it was like when polio was a day-to-day part of our lives. I remember my mother not permitting me to swim in the public pool because she was concerned that I might contract polio. As a child, I was frustrated, of course, because I wanted to learn how to swim. But as a mother, I can appreciate how frightened she was of the threat of polio.

The good news is that parents today do not have to worry about their children getting some of these preventable diseases. However, when parents cannot get the vaccines, they may doubt their necessity, since they have never seen the diseases for themselves.

The bad news is that we could be creating a situation where a generation of children are not fully vaccinated, a generation of children that is susceptible to diseases, diseases that our country has not seen in decades. We simply cannot let this happen.

Over the last several months, numerous constituents have raised the issue of shortages. Parents, doctors, and public health experts are all expressing frustration. They are asking the key question, what is going on here? I want to know the answer to that myself.

Given the progress we have made in this country toward immunizing children, and given what diseases could reemerge if vaccines are not consistently available, we need to shine the national spotlight on this issue.

That is why I approached Senator Lieberman about having this hearing, and I appreciate his leadership on this issue and the hard work that his staff has put into this. The purpose of today's hearing is to examine what is causing the shortage? What is the extent of the shortage across the country? And what is the government doing to address the problem and prevent future shortages?

Let me be clear. I see a role for the Federal Government in addressing the shortage, but this is a shared responsibility. Pharmaceutical companies, physicians, the public health system, and officials at all levels of government should play a role in ensuring that there is an adequate supply of vaccines. We need to work together to develop strategies and incentives to increase the vaccine supply in this country.

This is a complex issue with no easy solution. While the current shortage is likely to improve for next year, the underlying problems that have contributed to it will remain. That is why it is imperative that Congress take a hard look at this problem now. We need to work together with industry, physicians, and public health officials to find solutions that will ensure children's health and prevent vaccine shortages in the future. We cannot afford to ever let a generation of kids susceptible to these horrific diseases go unvaccinated.

I want to thank all the witnesses for being here today, and I look forward to learning from you how the shortage is affecting our Nation and hearing your suggestions on how we might be able to prevent shortages in the future.

At this time, I would like to call on Senator Bunning, if he would like to make an opening statement.

OPENING STATEMENT OF SENATOR BUNNING

Senator BUNNING. Thank you, Madam Chairman. The United States has done an exceptional job of eradicating and decreasing the prevalence of many of the life-threatening and debilitating diseases of the past, including polio, smallpox, rubella, measles, and others. Vaccinations are one of the most important things parents can do for their children and the health and well-being of their children.

Professionals spend a lot of time working with parents to make sure they know the proper vaccination schedules. However, the current vaccination shortage is risking the lives and health of many children, as doctors' offices and hospitals are delaying administration of certain vaccines because they simply are not in stock. This could cause many children to go without the necessary shots, which could lead to serious health problems in the future.

According to the CDC, there is currently a shortage of five vaccines that protect against eight diseases. It would be a tragedy if we saw a resurgence of any of the diseases we thought we had conquered.

As the witnesses today will testify, there are several reasons for the vaccine shortages, including increased liability, production problems, and changes in manufacturing requirements. I hope that

Congress can do its part to ensure that an adequate vaccine supply is available to parents and the doctors and health care facilities across this country.

While we work to address the current vaccine shortage, Congress also needs to make sure that families can afford them when they are available. In fact, this is an issue that I have been working on for the past several years, and last year I introduced legislation called the Vaccinate America's Children Act Now. This bill reduces the tax on vaccines to 25 cents per dose from its current 75 cents per dose and is designed to make vaccines more affordable to many American families, giving them one more incentive to adequately protect their children.

I am looking forward to hearing from our witnesses today about this important issue and appreciate the time and effort they have taken to be here today. Thank you, Madam Chairman.

Senator CARNAHAN. Thank you, Senator Bunning.

I would like now to proceed to our witnesses and to call our first panel. Joining us today are Dr. Timothy Doran from the American Academy of Pediatrics; Dr. Mary Anne Jackson from Children's Mercy Hospitals in Kansas City; and Wayne Pisano, Executive Vice President of Aventis Pasteur North America, representing the Pharmaceutical Research and Manufacturers of America. We welcome you.

Dr. Doran has been a practicing pediatrician for 20 years. Since 1999, he has chaired the Department of Pediatrics at the Greater Baltimore Medical Center in Maryland. Dr. Doran served as the President of the Maryland Chapter of the American Academy of Pediatrics from 1996 to 1998 and was honored as Pediatrician of the Year by the Maryland Chapter. Congratulations. He is currently the Chairman of the National Nominating Committee at the American Academy of Pediatrics.

Dr. Jackson has been a staff pediatrician at Children's Mercy Hospitals and Clinics in Kansas City, Missouri, since 1984. In 1996, she was appointed as Chief of the Pediatric Infectious Diseases Section. She is also a Professor of Pediatrics at the University of Missouri-Kansas City College of Medicine. Dr. Jackson is a fellow of the American Academy of Pediatrics and the Infectious Diseases Society of America, as well as a member of the Pediatric Disease Society.

Mr. Pisano, an Executive Vice President for Aventis Pasteur North America, has overall responsibility for both the United States and Canadian businesses. He joined the firm in 1997 as Vice President of Marketing and was promoted to Senior Vice President of Marketing and Sales the next year. Under his leadership, two of the company's key vaccines for polio and flu each achieved milestone sales levels.

Thank you all for being here. Dr. Doran, we have your prepared statement along with all the other statements from today's witnesses and they will be entered fully in the record. But I ask that you proceed with your oral statements for approximately 5 minutes. We have a light system here, as you can see, and it will let you know when you have 1 minute remaining. So we welcome your testimony today, Dr. Doran.

TESTIMONY OF TIMOTHY F. DORAN, M.D., F.A.A.P.,[1] CHAIRMAN, DEPARTMENT OF PEDIATRICS, GREATER BALTIMORE MEDICAL CENTER, ON BEHALF OF THE AMERICAN ACADEMY OF PEDIATRICS

Dr. DORAN. Thank you. Good morning, Madam Chairwoman and Senator Bunning. I am Dr. Tim Doran, a practicing pediatrician and Chairman of Pediatrics at the Greater Baltimore Medical Center, Community Hospital in Baltimore, Maryland. On behalf of the American Academy of Pediatrics, thank you for the opportunity to testify today about the current shortage of childhood vaccines.

My practice consists of about 1,800 children from predominately middle-class families. In the past, however, I have practiced in many different locales, from a poor island in the West Indies to the inner city of Baltimore. In the 20 years I have been practicing, I have never before experienced any vaccine shortage for a required childhood vaccine in this country.

This morning, I want to address three key points. First, I will describe the consequences of the vaccine shortage to patients and their families. Second, I will tell you about the administrative impact on pediatric practices which you alluded to before, Senator Carnahan. And finally, I will summarize the Academy of Pediatrics' recommendations to address this problem.

The heart and soul of a pediatrician's job is disease prevention. The predictable delivery of safe and effective vaccines is central to our goal of keeping children healthy. In recent months, my practice has seen shortages in several routinely administered vaccines, reflecting a national trend. In fact, currently, I am out of the new pneumococcal vaccine. This vaccine protects children from life-threatening meningitis, pneumonia, and blood infections. Many of my pediatric colleagues, such as those in Wisconsin, are also completely out of this vaccine.

A pediatrician from New Mexico reports that his high-risk population of American Indian infants is also currently out of this vaccine. This is especially troublesome because he recently diagnosed a 4½-month-old Navajo infant with a case of pneumococcal meningitis—a vaccine preventable, potentially fatal childhood illness.

The parents of my patients have been understandably anxious when they have learned that a vaccine is unavailable. They know that there is a small but finite chance that their child might become ill with an otherwise easily preventable illness because of a delayed or missed vaccine.

Because of recent media publicity and campaigns by anti-vaccine groups, I spend a significant amount of time with many parents reassuring them that our vaccines are safe and beneficial. They do not have the years of knowledge that the Senators on the Committee have. I cannot help but wonder that my credibility suffers when I then have to explain that these important vaccines are not available for their child.

In addition to the major risk to patients and worry to parents, the vaccine shortage has had an administrative impact on my practice, as well. We must now create a system of callback lists to reach those most in need of missed vaccines when they become available.

[1] The prepared statement of Dr. Doran appears in the Appendix on page 33.

My experience and that of other pediatricians has been that these systems are not very reliable or effective. Even in my relatively affluent practice, the level of compliance with these callbacks is far from perfect, and clearly inferior to immunizing at routine checkups.

I have also had to explore creative and time-consuming alternative methods to procure the full supply of vaccines that my practice needs. For instance, my recent experience is that buying directly from the pharmaceutical representatives is more fruitful than buying through the hospital pharmacy, which was my usual source. It is another reminder to me of the lack of a coordinated distribution system that has led to spotty supplies.

The bottom line is that the public requires a secure supply of all the recommended pediatric vaccines, vaccines that save children's lives and are the most cost-beneficial medical intervention in history. We must safeguard our children from preventable interruptions in vaccine delivery. This can never happen again in this country.

One immediate step is for the Federal Government to adequately fund the creation of stockpiles for all recommended vaccines, stockpiles of sufficient size to ensure that significant and unexpected interruptions in manufacture do not result in shortages for children.

Another step is to preserve and strengthen the liability protections for consumers, manufacturers, and physicians through the Vaccine Injury Compensation Program. The VICP has been an integral part of maintaining the vaccine market. Enacted in the late 1980's with the support and guidance of the American Academy of Pediatrics, the VICP has helped to stabilize what was then, and appears to be again, a fragile vaccine market.

The American Academy of Pediatrics has participated in the work of the National Vaccine Advisory Committee. We have seen the draft report presented at NVAC's recent meeting. That report offers a good starting point toward fixing an absolutely fixable problem.

Universal immunization made a profound improvement in the health of our Nation. It would be tragic to let this hard-won advance slip away and jeopardize such a fundamental public health measure. The health of our children depends on it. Thank you for your time and attention.

Senator CARNAHAN. Thank you, Dr. Doran. Dr. Jackson.

TESTIMONY OF MARY ANNE JACKSON, M.D.,[1] CHIEF, PEDIATRIC INFECTIOUS DISEASES SECTION, CHILDREN'S MERCY HOSPITALS AND CLINICS

Dr. JACKSON. Madam Chairwoman and Mr. Bunning, I am Dr. Mary Anne Jackson, Professor of Pediatrics and Chief of the Section of Infectious Diseases at the Children's Mercy Hospitals and Clinics in Kansas City, Missouri. Our pediatrician center is the only children's hospital between St. Louis and Denver. We serve a 140-county region and we see over 300,000 children per year.

[1] The prepared statement of Dr. Jackson appears in the Appendix on page 39.

My role is as a pediatric infection specialist. I provide care and consultation for a variety of children, many of whom are otherwise healthy children, hospitalized with serious and sometimes life-threatening infections, such as meningitis. Some are children with underlying diseases such as AIDS, cancer, prematurity, those with transplanted organs, who have a variety of complex infections. I am a clinical researcher and my research focus is on emerging infections, bacterial resistance, overuse of antibiotics, and prevention of communicable diseases.

My third role, and possibly my most important role, is as an advocate and educator for children's health issues. As a community resource, my colleagues and I speak formally to groups of pediatricians locally, regionally, and nationally. On a daily basis, community pediatricians call us with specific questions regarding their patients, perhaps about the diagnosis and treatment of a child with a diagnostic dilemma, questions regarding antibiotics, but fully 25 percent of those phone calls sometimes are related to immunization issues.

When I lecture on immunizations, one of my key messages is that physicians must maintain timely immunizations as a high priority in the care of infants, children, adults, and adolescents. I am preaching to the choir when I tell pediatricians that we have eradicated or nearly eradicated diseases, as you all know, diphtheria, measles, mumps, polio, rubella, and tetanus.

Ask any pediatrician who trained in the 1970's and 1980's and they will no doubt remark to you that one of the most remarkable accomplishments of their career is the eradication of Haemophilus influenzae Type B infection, which was the most common cause of meningitis up to approximately 1993. Within 3 years of the implementation of that vaccine, this disease virtually was eliminated and I have not seen a case in almost 10 years. However, I remind pediatricians that these pathogens continue to persist in the United States and in other countries and that our immunization program, I would consider fragile, at best.

In the United States, only 80 percent of children are adequately immunized. In the State of Missouri, we are at the national average. In the Kansas City area, devoted efforts from organizations such as the Partnership for Children and the Mid-America Immunization Coalition have worked tirelessly, and we have raised immunization rates from a pitiful 50 percent in 1990 to 85 percent in the year 2000, but we still have disparities where counties have immunization rates as low as 66 percent.

I remind pediatricians that we cannot be complacent, because I continue to see children with vaccine-preventable diseases. Since I have come to Children's Mercy Hospital, we have diagnosed over 300 children with whooping cough. Most recently, we had a 2-month-old in our intensive care unit for over a month with complications of this infection. In the last year or so in my community, a child has died with chicken pox complications, a child has died of pneumococcal meningitis at the age of 5 months, and a very sweet 15-year-old boy in May 2001 died of liver cancer, a complication of hepatitis B virus that was transmitted at birth. All of these were vaccine-preventable diseases.

This unprecedented and unanticipated shortage of routinely recommended vaccines has resulted in inadequate supplies of actually 8 of the 11 routinely administered vaccines, and shortages are more acute in the public sector than the private sector, and this is important for us, Senator Carnahan, because 50 percent of the children in the State of Missouri are covered under the public sector Vaccines for Children program.

The vaccine shortage has impacted the physicians' ability to provide a consistent recommendation and practice for vaccine implementation. We also keep a log, and we try to call back. We have tried to follow the CDC's guide for prioritization of vaccines, but we cannot do this. Most physicians in our areas do not. Forty percent of physicians nationally do not. Suddenly, physicians realize that they are out of a certain vaccine or it is not practical to triage vaccines in the course of a busy pediatric practice. We have also changed our immunization requirements in the State such as we tell pediatricians in July 2001, you must have varicella vaccine to go to day care. Less than a year later, we tell them, never mind.

What is the impact of the vaccine shortages? We estimate that the negative impact is a decline of almost 10 percent at this point. I tell pediatricians that children who start their vaccines on time are clearly more likely to be current throughout their first year. Our message to the public and professionals becomes muddled, though, when we document the scope of disease that can be prevented by immunization and then delay and defer opportunities.

Prevention of infectious diseases by immunization has been one of the great public achievements of the 20th Century. Whether our current vaccine shortage is related to companies leaving the market, manufacturing and production problems, or insufficient stockpiles, it is clear that one of the indelible marks of this shortage is that parents and professionals are confused and frustrated and all strides made in the last decade may go by the wayside. Our goals should be to maintain a supply of licensed vaccines that are safe and effective. These vaccines should be available for every child and adult in the United States. Vaccine research development and production must be enhanced.

And last but not least, we must renew our educational efforts following the correction of this shortage to ensure that our children are healthy now and as we face the challenges of the future.

Our promise to parents should be resolute. A strong immunization program needs to be ensured. It is the right action and one of the most cost-effective means of ensuring the health of children in our country.

Senator CARNAHAN. Thank you very much. We will move on to Mr. Pisano.

TESTIMONY OF WAYNE F. PISANO,[1] EXECUTIVE VICE PRESIDENT, AVENTIS PASTEUR NORTH AMERICA, ON BEHALF OF PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA

Mr. PISANO. Good morning, Chairman Carnahan, and Senator Bunning. On behalf of the Pharmaceutical Research and Manufac-

[1] The prepared statement of Mr. Pisano appears in the Appendix on page 43.

turers of America, PhRMA, I am pleased to appear at this hearing today on childhood vaccines. I am Wayne Pisano, Executive Vice President of Aventis Pasteur.

PhRMA represents the country's major research-based pharmaceutical and biotechnology companies which are leading the way in the search for new cures and treatments that enable patients to live longer, healthier and more productive lives. More specifically, PhRMA represents the four companies supplying 100 percent of childhood vaccines in this country and 90 percent of all vaccines. Many people are surprised that the industry is so small, but the fact is, the liability crisis of the 1980's drove many companies out of the market. I will talk more about that later in my testimony.

We are all keenly aware of the vaccine shortages facing our Nation today. The good news is that most of these shortages have been or will be resolved this year. In the long term, we need to understand what causes vaccine shortages and what can be done over the long term to alleviate them. I will outline six proposals to alleviate shortages in the long-term.

But first, I want to talk about the vaccine industry and what is unique about it. First, unlike pills, vaccines require the use of biological organisms, viruses and bacteria, which will not always grow or respond on demand.

Second, vaccines are difficult and time consuming to produce and the regulatory approval process for new vaccines and for changes to existing vaccines is highly complex and lengthy, with timetables that are difficult to predict. The process is regulated such that every lot of vaccine must be approved by the manufacturer and released by the FDA. Taking into account that production schedules can run 12 months and longer, any abrupt change in policy that can influence demand or move a company to leave the field can result in supply interruptions.

A good example is the decision to remove thimerosal, a preservative, from vaccines. The decision was made to remove thimerosal, which had consequences exacerbating a shortage of a childhood vaccine, DTaP. Thimerosal is a preservative which allowed health care providers to purchase and use multi-dose vials. Without thimerosal, single-dose packaging must be used. The manufacturing process for Aventis Pasteur had to be changed and approved by the FDA. The process changes lengthened the manufacturing time lines and manufacturing yields dropped, since it is necessary to over-fill every single vial to assure the provider can remove a full dose.

The resulting shortage should be alleviated by the fall, if not this summer, and providers should be able to provide all five doses require for the pertussis schedule. In part, this is because the FDA recently licensed Aventis Pasteur's Canadian DTaP product, DAPTACEL, for use in this country.

Third, vaccines are tremendously undervalued as preventative measures. Prices can best be categorized as commodity-like, compared to much higher prices for other forms of medicine. Public purchasing entities continually endeavor to drive down the price the government will pay for vaccines despite the fact that, in many cases, a dose or series of doses of vaccines provides a lifetime of protection against a disease. This is occurring at a time when man-

ufacturers are investing significant resources to meet the current good manufacturing practices standards set by FDA.

Before I outline the six steps to a stronger vaccine supply, let me state what is not needed. First, what is not needed is a government-built vaccine facility, GOCOs. These would take years to develop and face the same problems as private facilities. In addition, they would dampen incentives for new private entrants to enter the vaccine business. It is often forgotten that it is science, not manufacturing, that is the limiting factor in developing new vaccines. All the manufacturing capacity in the world cannot produce a vaccine until the science is there.

Nor do we need a new centralized vaccine authority. The FDA and CDC's regulatory regimen is comprehensive and well-established, and there is no compelling reason to develop a wholly new system.

We do have a number of suggestions which we believe would help meet our vaccine supply needs in the future. Here are the six initial proposals. We support expanded stockpiles for use if supplies are disrupted. We support additional funding for the CDC to establish stockpiles for both single- and multi-source products. For example, had there been a national tetanus stockpile, we would not have had the shortages we recently experienced when one company left the manufacturing process, leaving it to a single manufacturer.

No. 2, use the expertise of the vaccine manufacturers to help formulate sound immunization policy. Manufacturers can provide realistic assessments and expertise about how vaccines are developed and produced, the challenges in doing so, as well as a view into how providers practice and use vaccines. It is important that those making vaccine policy in government have this expertise available to them. However, in more formalized settings, this is no longer occurring. An example is CDC working groups where industry representatives are no longer permitted to participate in discussions. Industry does not expect to participate in decisionmaking issues, but given the limited universe of vaccine expertise, governments can benefit from the use of vaccine expertise in this industry.

No. 3, government and advisory bodies need to act with greater flexibility. Continued uninterrupted manufacturing and distribution of vaccines is dependent upon predictable action by government agencies and advisory committees. Specifically, we suggest that government agencies and advisory committees need to allow adequate advance notice whenever manufacturing changes are necessary. Simply put, if change is required before manufacturers can make them and the FDA can approve them, shortages will occur.

No. 4, the Vaccine Injury Compensation Program, VICP, should and needs to be strengthened. The Vaccine Injury Compensation Program stabilized our national immunization program since the late 1980's, reducing the frequency of liability uncertainty that has destabilized our industry. VICP provides a system of compensation for injury claims should they be litigated within the VICP system.

Recently, new strategies have emerged to circumvent the program. Once again, manufacturers are facing liability exposure that measures in the billions of dollars. Already, we are facing millions of dollars in costs to defend against specious claims. Recently, Senator Frist introduced a thoughtful and comprehensive vaccine bill,

S. 2053, which contained a section on VICP. It adopted the recommendations of the Advisory Commission on Childhood Vaccines to make the system more user friendly. In addition, it reiterated the intent of the VICP that claims processed should proceed initially through this program. We strongly commend the provisions of the Frist bill to you. We are pleased that last Thursday, ACCV adopted virtually all of Senator Frist's proposals.

No. 5, to strengthen our message that prevention is the most desirable intervention, a reorientation of health care priorities to emphasize prevention over cure will provide incentives to doctors to immunize patients and to manufacturers to maintain their commitment to vaccine production. There needs to be sufficient payment for preventative services. Recent reductions in CMS reimbursement are disincentives to physicians. Reimbursement rates should reflect the full value of vaccines, including a realistic administration fee for physicians.

And No. 6, heed the warning signs of a real and present danger, increasing lack of confidence in immunization. The good news is that parents no longer fear many infectious diseases because of the success of our immunization programs. They also have lost the respect for the importance of immunization as they have lacked the firsthand experience or knowledge of the devastating damage vaccine-preventable diseases can cause. We urge you to look at ways to bring the public into the process and boost its confidence in the immunization system.

The vaccine enterprise in this country is a remarkable success story. I do not believe it is fragile, yet it clearly has several areas that can be strengthened. I hope you will give consideration to the proposals we have laid out. Fortunately, we have an industry that wants to partner with government and with all elements of our Nation's immunization enterprise to achieve even greater successes.

Thank you very much for your attention and your commitment to the immunization system in this country.

Senator CARNAHAN. Thank you, Mr. Pisano.

I would like now to open our questioning by addressing the impact of the shortage is on children. I would like to raise the issue of what happens to children when they miss their vaccines.

Dr. Doran, I am concerned about the issue of children slipping through the cracks. I know from personal experience, most private physicians do not have a system to make sure that a kid who has missed a vaccination gets back into the office once the vaccine does become available. This issue is particularly problematic for children whose only health care is through the public health system. They may visit different health clinics for their medical needs and so the physician helping them will not have access to a complete medical record of that child.

Can you comment on your own experience with this issue and what you are hearing from other physicians as to what they are experiencing, and are you receiving any Federal guidance or assistance to help with this problem?

Dr. DORAN. Thank you, Senator Carnahan. It is a multi-faceted answer, and I will begin by saying that one of the problems in this whole past year of shortages has been the spottiness and the fact that we have had multiple vaccines available or not available for

different lengths of time. So planning has become problematic in that we cannot set out a plan without changing it in a month because a vaccine either becomes available or not available.

The current practice and those of the colleagues I have talked to, both in the public and private sector, has been to create lists of patients when they come in, to take their phone numbers and keep them in a log, and as the vaccine comes in, to try to contact those patients to bring them back in. As you can imagine, that is a difficult task. Parents have to take off work to come in and get the vaccine. It is not part of their regularly scheduled vaccination schedule and it is difficult. I cannot give you specific numbers in terms of how effective that system is other than to tell you it is far from perfect.

I have created a system in my office. I actually have a web page and people can register on that web page and I can then E-mail them, sort of broadcast E-mail them to notify them when vaccines are in, but that is very new and, obviously, not everybody has access to the Internet.

It is just a problem. I think, talking to all my colleagues, my impression is that the majority of kids are probably waiting until their next scheduled visit before they get the vaccine, so if they have missed a pneumococcal vaccine at 2 months of age, they are probably not receiving it until their 4-month check-up, which is the next regularly scheduled visit, rather than at 3 months if the vaccine happened to come in in the interim. Most parents will probably wait.

I have a bunch of anxious parents who will come in very quickly, but for most parents, it is a lot of work to get to the office, both working class parents or middle class parents. It is very difficult to spend the time and get to the office in order to get that vaccination.

Senator CARNAHAN. So it is a lot better to do it on a regularly scheduled basis than to have to make the time.

Dr. DORAN. Absolutely.

Senator CARNAHAN. Dr. Jackson, I think parents are receiving something of a mixed message about vaccines. They are being told how important they are for their children's health, and then when they go to a doctor's office, they are being turned away. Can you address the impact that this is having both on parents and public health overall?

Dr. JACKSON. Well, I think I can start by saying that as new vaccines have been licensed and we have educated parents and professionals in our community about those vaccines, there have sometimes been a lag period before these immunizations are even embraced when we have them available. The examples I would give you would be hepatitis B vaccine and varicella vaccine, where it took 2 to 5 years before parents and professionals really embraced these vaccines and they began to be reliably used.

I think you are entirely correct that I call this a muddled message. We cannot tell parents that we continue to see vaccine-preventable disease, that we continue to see vaccine-preventable deaths, and make no mistake, this is not a Kansas City phenomena. This is not a Missouri phenomena. This is a national phenomena. We cannot tell them that this risk is just for their child

and then tell them that we do not have vaccines available, to come back when we call them on the telephone. In the public sector, we are lucky to even have patients with telephones or with an accurate telephone number.

So I think that one of our greatest problems will be, if we are able to correct this, and I feel that we are, we will have the American public that has lost confidence or become complacent about immunizations and that our efforts to educate both parents and professionals will have to be renewed. We will have to remind people that not only are there communicable diseases in this country that can be prevented by vaccine, but we will have to remind them once again that timely immunization should be a high priority for all.

Senator CARNAHAN. I understand that there are a number of collaborative efforts that are going on around the country to increase immunization, and it is my understanding that Kansas City is about to launch such a campaign. I was wondering if you could discuss the "Give Life a Shot" campaign, what its purpose is and what impact you think it will have considering the current vaccine shortage.

Dr. JACKSON. The Hallmark Foundation in Kansas City has awarded a grant to both the Children's Mercy Hospital and to the KU Medical Center pediatricians to develop an educational plan for our community. It will consist of public service spots. There will be signage on public transit systems, basically to remind families to insist that their children start vaccines on time at 2 months of age.

There was one or more individuals within our group who suggested that perhaps this is not a good time to educate the public because how can we say, immunize on time, start at 2 months, and then have them come in and say, we do not have these vaccines available? My response to that, though, is we must continue our efforts to educate the public, and as we do see perhaps an end to this by the end of the year, perhaps by summer for many of these vaccines, by the end of the year 2003, I think we must continue to educate the public and our campaign will start in August.

Senator CARNAHAN. Thank you. Next, I would like to address a few of the factors that affect the supply of children's vaccines. One important issue is the amount of production capacity that exists and whether it is sufficient to meet the demand.

Mr. Pisano, some pediatricians say that the current shortage in childhood vaccines is the worst shortage they have seen in their entire careers. I think Dr. Doran expressed that. Twenty years ago, there were 18 companies manufacturing vaccines, and in the 1980's, there were seven companies. Today, we have only four companies making vaccines for children in the United States.

I am concerned whether the country's physical infrastructure to manufacture vaccines is sufficient to meet the demand for the long term. Does our country have enough production capacity to make the demands that we need, and if more companies do not enter the market, will we be able to meet demands for vaccines in the future?

Mr. PISANO. I think that the current manufacturing capacity in some situations is inadequate. I think the example of Td met that

definition, where one manufacturer left the industry and the remaining manufacturer did not have the capacity at that time.

Now, I think what we have seen from the four manufacturers is a renewed commitment and expansion of capacity. We have seen one manufacturer expand their capacity for pertussis vaccine, another manufacturer license a second facility for pertussis vaccine. We have seen expansion on Td vaccine capacity, and we are also seeing now further expansion for the pneumococcal vaccine.

So I think the industry is responding, and I think we also will be seeing other manufacturers looking to enter the U.S. market and will be taking their products through the clinical and development process and filing for registrations with the FDA. So I think the problem is on the table now, and I think the industry is responding. The immediate shortage should be over for most of the vaccines this summer, and definitely by year end for all the pediatric vaccines, and then the infrastructure will continue to expand from there.

Senator CARNAHAN. As you pointed out, the immediate shortage is likely to be over sometime during the summer, but I am concerned that the underlying factors that have contributed to the shortage will remain. Supply and demand will remain tight with little room for error. There will still be only four companies manufacturing all the childhood vaccines in the country and there will still be several vaccines that only one company will produce. So any problem will have a significant effect on the supply.

I think a key to finding a long-term solution to this is increasing the number of the vaccine manufacturers in the market. What can be done to encourage more companies to enter the vaccine market?

Mr. PISANO. I think there are a number of factors on why companies enter and leave markets. One has to do with the risk and liability associated with—that the vaccine manufacturers are subject to, and the Vaccine Injury Compensation Program is something that needs to be strengthened so manufacturers are not threatened by these specious claims and billions of dollars of lawsuits, because that clearly discourages people from entering the marketplace.

Another is, I think we need to have an appreciation in the United States of the value of vaccines. Vaccines are not valued the way pharmaceutical products are valued, and so prices are driven down. They are very commodity-like, and in order to meet the current good manufacturing practice standards that are set, companies have to invest in their manufacturing facilities. Many of these facilities are old facilities for vaccines that were licensed 20, 30, or 40 years ago, and it is not cost-effective for the manufacturer to do that. It is too costly because there is just not enough return for them on making that investment.

Senator CARNAHAN. If a company is experiencing a production problem or they know that they will stop manufacturing a vaccine, could a shortage be avoided if the government and other manufacturers were given advance notice? Could you explain how you would propose this would be addressed?

Mr. PISANO. I can speak on behalf of Aventis Pasteur specifically on that. A proposal that we have brought forward to the other vaccine manufacturers that is still in discussion is allowing the CDC to be a clearinghouse for confidential information in terms of man-

ufacturing issues such that they would have the ability to do one of two things. They could ask another manufacturer to increase production when we have multi-source products, or they could draw on their stockpile, and I think stockpile has been mentioned by several people today.

We truly believe that we need to have an adequate stockpile, because when you are dealing with biologics, there is always the risk that there will be a manufacturing issue somewhere in the future and having a stockpile provides us the cushion necessary to get through those types of issues.

Senator CARNAHAN. Thank you. I had just one other question and then I will turn the questioning over to Senator Bunning.

For Dr. Jackson, are you seeing vaccine-preventable diseases reemerge, and if not and the shortage continues, how long do you think it would be until we do begin to see these diseases again?

Dr. JACKSON. It is hard to say of vaccine-preventable diseases reemerging at this point. We clearly continue to see vaccine-preventable diseases. I used pertussis as one example. We continue to see children with complications of chicken pox, albeit fewer than we did, say, in the early 1990's.

I think as immunization coverage rates fall, though, and I think as they fall below 80 percent is when we risk the emergence of vaccine-preventable diseases. I mentioned to you that nationally, we are at about 80 percent, in Kansas City, perhaps 85 percent. That is why I described our program as fragile. I think that if we decrease by 10 percent, then we are at 70 percent, and then I think that, clearly, we will see the emergence of vaccine-preventable diseases.

What is even worse is that we have recently had the licensing of the new pneumococcal vaccine, and it has been embraced very quickly by pediatricians who do see children with pneumococcal pneumonia bloodstream infection and meningitis. They recognize that disease and the need to prevent it. Almost months after we start the implementation of that vaccine, it is taken away from us, and it is probably our greatest shortage right at this point. We currently have none at the Children's Mercy Hospital for our Vaccines for Children Program.

Senator CARNAHAN. Thank you. Senator Bunning.

Senator BUNNING. Thank you, Senator.

Dr. Doran, in your practice, how often do you not have the necessary vaccines? You told us about how you try to follow up, but knowing full well, having had nine children and having gone through the vaccination process with those nine children, and fully aware of the fact that a smallpox vaccination only lasts 10 years, and so all of us sitting in this room are not immune to smallpox because if you have not had one recently, you are not immune, so tell me about how often do you not have the necessary vaccine.

Dr. DORAN. I would be delighted to. If I could just mention one thing about Senator Bunning. As a 7- or 8-year-old, my very first major league baseball game was at Fenway Park when Senator Bunning threw a no-hitter.

Senator BUNNING. You are a New Englander, then?

Dr. DORAN. As a 7-year-old, I was——

Senator BUNNING. From the State of Maine.

Dr. DORAN. As a 7-year-old, I was upset that the Red Sox lost, but that has been a chronic problem. [Laughter.]

Over the past year, I have not had a reliable supply of tetanus vaccine. Actually, I was mentioning to the other panel members, this past week, I received my first shipment of adult tetanus vaccine that I have had in months and months. I have had shortages of varicella vaccine, of MMR, of DTaP, and the worst has been the pneumococcal vaccine.

They have been for varying periods of time. The tetanus has been for the entire period. I have been out of the pneumococcal vaccine probably 20 percent of the time. Varicella was brief for me. It was probably 3 to 4 weeks over the past year, and MMR and DTaP, probably of similar length of time that I have had shortages.

Senator BUNNING. Did you have problems with the flu vaccine last year?

Dr. DORAN. Yes.

Senator BUNNING. Because we had problems here in the Capitol with it.

Dr. DORAN. Yes. In my testimony, I mention the required childhood vaccines. Flu vaccines have been a problem off and on over the years, and I certainly have had shortages of flu vaccine. But of the potentially lethal diseases in childhood and the required—it is not one of the required childhood vaccinations. It is for high-risk children that we see, so we do have recommendations——

Senator BUNNING. And for seniors.

Dr. DORAN [continuing]. For seniors and for health care workers, actually, who work with immuno-compromised patients. So I have seen those vaccine shortages, but I think that, for pediatricians, the shock this year is that not just one vaccine has been short, but as you mentioned, five vaccines containing eight preventable illnesses in them have been short, and it has clearly been—we have depended on this. It has been so reliable, and then to have such a disruption in the supply has been very frustrating and very difficult to deal with.

Senator BUNNING. Dr. Jackson, let me ask you, parents and confidence, there seems to be a disconnect. Our parents, or my parents, there was no hesitation at all as far as polio, as far as smallpox or whooping cough or whatever it was. When we went to the doctor and the vaccination was available, they gave it to us, and on a systematic basis. If public health facilities were available, those who could not afford it privately got it at public health facilities. Tell me if the same confidence exists now between parent and physician and vaccinations, because I suspect that it does not.

Dr. JACKSON. And it is somewhat different, Senator Bunning. Nowadays, parents are part of the health care system. So when a child comes to your office for immunizations, we do not just give the vaccines, we tell them what vaccines they are receiving, we tell them why they are receiving their vaccines, we discuss risks and benefits of vaccines, and so perhaps that is better in this day and age.

But the confidence issue comes into call when we tell them why they are receiving vaccines, the risks and benefits of vaccines, that we recommend these vaccines and then we are unable to provide

them those vaccines. So that is the confidence issue that has occurred.

Complacency, I think, is the big risk, and it is not because the professionals will lose their focus. It is not because the parents will lose their focus, which is keeping children healthy and preventing communicable diseases. It is because we have developed this routine of promising something that we cannot make good on, and so I think we need to make good on our promise.

Senator BUNNING. I agree with that 100 percent, but the fact of the matter is, the parents' awareness and the trust factor in the vaccinations, without having, in other words, like the anthrax in the military, for instance. A lot of people were required by the military to get anthrax vaccinations and they said, no, we do not want to take the risk because we think this vaccination or vaccine is not something that we should do. How much do you have with parents as far as children's diseases and vaccinations are concerned?

Dr. JACKSON. I see your question. When we say to a family, this vaccine is safe and effective, do they believe us? Do they have confidence?

Senator BUNNING. That is right.

Dr. JACKSON. Exactly. I would say the vast majority of parents that we encounter do have confidence in their pediatrician to provide them with the best information possible. We have a segment of the population, perhaps 10 percent, who are highly concerned and need more reassurances that we are convinced that this is the right thing to do, and then there is a small segment of the population that are truly anti-immunization and may not be willing to hear evidence-based information that science tells us that there is no connection between, for instance, autism and MMR. I think that is a small segment of the population. I think the vast majority of parents have confidence in their pediatricians, like Dr. Doran, like pediatricians through our Children's Health Care Center.

Senator BUNNING. The only people we miss are those who never get there.

Dr. JACKSON. Correct, and that is——

Senator BUNNING. In other words, we do have a segment of the population that does not have them available to them because they do not get the public health links or they do not get the private physicians.

Dr. JACKSON. And that is where I think prioritization is an issue and falling through the cracks. In some of our populations in the public health sector, we have children who are living in circumstances that are unbelievable. They do not have electricity. They may not have a meal that day. They do not have clothing. I mean, for you to tell them that it is a priority for them to get their immunization gets washed out by the really important issues in their lives.

Senator BUNNING. The only time probably we see them is when they get to school.

Dr. JACKSON. Exactly, and that is why our Give Life a Shot program is going to focus, hopefully, on that hard-to-reach population.

Senator BUNNING. Mr. Pisano, let me talk to you. You mentioned the fact that the threat of class action lawsuits against manufacturers could threaten vaccination or vaccine production. You also

said that the Vaccine Injury Compensation Program needs some changes. I would like for you to expand on that.

Mr. PISANO. I think it is important for any litigation in terms of harm from vaccines or perceived harm from vaccines must go through the Vaccine Injury Compensation Program, and today, we are finding the lawyers working around the system and going directly into the State court systems and suing the manufacturers directly. Right now, there are class action lawsuits that total in the billions of dollars that the vaccine manufacturers are facing. The defense for these lawsuits is well into the millions of dollars already and we have just begun, and these are popping up every day across the country.

Senator BUNNING. Let me also ask, did you mention the fact, or did I read it in your testimony, that the industry representatives are no longer permitted to fully participate in CDC's working groups?

Mr. PISANO. That is correct.

Senator BUNNING. Give me some kind of background and explanation on that.

Mr. PISANO. I think we are in an era where there is concern about manufacturers' interests and bias. Obviously, we are in business to manufacture pharmaceuticals and vaccines, and we have been distanced from these working groups. We are allowed to make a statement in a public forum, but we are not allowed to participate in the discussions that go on behind closed doors. We believe that we have information that would help the working groups make better decisions.

We also realize we should not be part of the decisions, because we do have an interest in the outcome of the decision. But information in terms of manufacturing capacity, information in terms of how fast we can change a formulation to take a preservative out of a vaccine and go to a preservative-free formulation. We had working groups that made recommendations to remove thimerosal. That was implemented before manufacturers could complete that removal and before the FDA had time to review that new formulation.

Senator BUNNING. Did that slow down, then, the manufacture of that vaccine, when you had to convert? Or were your production facilities, whoever it might have been, able to adjust to that in a reasonable manner?

Mr. PISANO. The removal of the preservative definitely slowed down the manufacturing process. We had to reformulate the vaccine, which, in essence, is like a full development program. It took 2 years. The recommendations went in place in about 15 months, and so there was a gap and that contributed to the shortage of the pertussis vaccine, which is where we believe the industry can help advisory bodies, working groups, by bringing that type of knowledge to the table. We do not disagree with the decision of the working group. We simply believe that we have information that will help them make a better sound decision.

Senator BUNNING. This is the last question I have for the two doctors. What will need to be done to make sure that all children are properly vaccinated once the shortage is over, especially for families who do not have a regular doctor and instead rely upon

health clinics and hospitals for their care? Either of you can try to help us out so we can do something.

Dr. DORAN. There clearly needs to be the kind of outreach programs that Dr. Jackson mentioned. The American Academy of Pediatrics, for instance, has joined with McDonald's to promote vaccinations, and there really has to be a much more proactive public health sector campaign to bring these children in.

We need to, obviously, as part of that, shore up the issues with preventing shortages, and the other thing that was mentioned by Mr. Pisano which will be important is to make sure that physicians' time and energy is adequately compensated. There are proposals to reduce the administration fee for vaccines to a level that would be, for pediatricians and for public health clinics, where they would be losing a significant amount of money every time they are giving a vaccine. So those types of reimbursement issues are key, too.

But in terms of reaching those hard-to-reach children, it is a matter of public will and campaigns to reach those children and to get them in.

Senator BUNNING. Dr. Jackson, do you have anything to add?

Dr. JACKSON. I agree that in this country, we need to prove to the American public that we value vaccines, and in doing so, we need to commit funds to the research and development of new and better vaccines. We, of course, need to continue our efforts to educate the public. We need to have immunization registries which are available which will allow us to share information confidentially about the immunizations that a child has had.

For instance, you are so right when you say that a child may be immunized in three different health departments and maybe two different physicians' offices. We see physicians' offices now not stocking vaccines because they are not being fairly compensated. It costs them $58 to buy the vaccine. The insurance company will reimburse them $48. And you multiply that by the number of patients that are seen in a pediatric practice and you can see why some practices are doing this.

And so we will have a child who comes in where we have no clue the number of vaccines they have received, the timing of those vaccines, and so I think that is one thing that we can do, also.

Senator BUNNING. Thank you, Madam Chairman.

Senator CARNAHAN. Thank you, Senator Bunning, and I thank our distinguished panel today, Dr. Doran, Dr. Jackson, and Mr. Pisano. Your willingness to be here has certainly helped us to have a better understanding. You have shed light on a very critical and very important issue in our Nation, and we appreciate you sharing your expertise with us. Thank you.

Our second panel will have two witnesses, one of which has not arrived yet but is on his way. One will be Dr. Lester Crawford. I will proceed with introducing him, even though he has not joined us yet. He is from the Food and Drug Administration, and Dr. Orenstein from the Centers for Disease Control and Prevention.

Dr. Crawford is the Deputy Commissioner for the Food and Drug Administration and has extensive experience in FDA matters. His previous government experience included serving as the head of the FDA Center of Veterinarian Medicine and as Administrator of the

Department of Agriculture's Food Safety and Inspection Service. During his 10 years at FDA and the Agriculture Department, Dr. Crawford has played major roles in mandatory nutrition labeling, the General Agreement on Tariffs and Trade, and the control of chemical and microorganisms in the food supply.

Dr. Orenstein is the Director of CDC's National Immunization Program and has a background in pediatrics and pediatric infectious diseases. Dr. Orenstein has spent more than 24 years at the CDC working in immunization and has been Director of the National Immunization Program since its founding in May 1993. He also serves on the National Vaccine Advisory Committee and the Committee on Infectious Diseases of the American Academy of Pediatrics.

Thank you for being here, and we will start, Dr. Orenstein, with you for an opening statement.

TESTIMONY OF WALTER A. ORENSTEIN, M.D.,[1] DIRECTOR, NATIONAL IMMUNIZATION PROGRAM, CENTERS FOR DISEASE CONTROL AND PREVENTION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. ORENSTEIN. Thank you very much. Good morning, Senator Carnahan and Senator Bunning. I am Dr. Walt Orenstein, Director of the National Immunization Program at the Centers for Disease Control and Prevention. Thank you for inviting me to testify about the current childhood vaccine shortages.

There are currently supply problems with five vaccines that provide protection against 8 of the 11 vaccine-preventable diseases of childhood. The current childhood vaccine shortages are unprecedented, and health care providers and parents have been justifiably frustrated. The Department of Health and Human Services takes these concerns very seriously, and CDC is monitoring the situation in a variety of ways.

I would like to point out some good news. Current information from the manufacturers indicates that many of these shortages will be over before the end of the summer.

The causes of the childhood vaccine shortages are multi-factorial and complex. Economic issues are clearly critical to the long-term viability of the vaccine industry. There is no single characteristic at the root of the current shortages. Some contributing factors include manufacturers' production capacity, regulatory compliance issues, manufacturers' business decisions to stop producing certain vaccines, and decreases in production yields caused by changing to single-dose vials to remove the preservative thimerosal from one of the vaccines.

The impact of the shortage is being felt by health care providers, schools, and parents. The vaccines most affected are the tetanus and diphtheria and pneumococcal vaccines, which both show about a 40 percent decrease in doses distributed nationally. School immunization requirements have also been affected because supplies have not been adequate to ensure that children in need of immunizations can get them.

[1] The prepared statement of Dr. Orenstein appears in the Appendix on page 54.

While it is impossible to predict the larger public health impact of the current childhood vaccine shortages, there is clearly an increase in vulnerability to disease when children remain unvaccinated.

In general, manufacturer projections indicate that the situation is rapidly improving. The most serious and enduring problem appears to be with the pneumococcal conjugate vaccine. According to manufacturer projections, this vaccine may be in short supply into 2003.

CDC and its partners are addressing these shortages in several ways. The Advisory Committee on Immunization Practices, with concurrence from the American Academy of Family Physicians and the American Academy of Pediatrics, has made several temporary changes in routine immunization recommendations. These changes prioritize limited vaccine supplies to the most critical doses in the schedule to the most vulnerable children. CDC is also monitoring State vaccine orders to help assure that vaccines in shortage purchased through our contracts are distributed equitably.

The CDC is in frequent communication with a wide range of partners regarding the status of vaccine production. CDC provides weekly vaccine supply updates on its website. This information is intended to help States and health care providers plan their immunization strategies.

In addition to working with other HHS agencies, such as the FDA and the Centers for Medicare and Medicaid Services, CDC is working with its partners in industry and with other groups to better understand the current shortages, identify potential short-term solutions, and prevent future shortages.

For some vaccines, CDC has maintained storage and rotation contracts, frequently referred to as stockpiles, which have been very effective in the past in alleviating brief disruptions in vaccine supply. These stockpiles are an important resource to maintain. Between 1984 and 2002, CDC stockpiles were drawn on multiple times when supplies of four different vaccines were interrupted. However, managing stockpiles effectively presents unique challenges and stockpiles are not available for four of the five vaccines with current vaccine supply problems.

In addition to the input CDC is gathering from its partners, the National Vaccine Advisory Committee and the U.S. General Accounting Office are conducting independent reviews. CDC looks forward to reviewing their final reports.

In conclusion, the current childhood vaccine shortages are complex, unprecedented in scope, and result from a number of factors. CDC has implemented several short-term measures to facilitate the efficient and effective use of available vaccines, and CDC is also receiving input from external organizations regarding strategies to prevent such shortages in the future.

Thank you for the opportunity to tell you about the current shortages. At this time, I would be happy to answer any questions.

Senator CARNAHAN. All right. Thank you.

Joining our panel will be Dr. Jesse Goodman. He is Deputy Director for Medicine at the Center for Biologics Evaluation and Research at the Federal Food and Drug Administration and he will

be speaking on behalf of FDA. Thank you, Dr. Goodman, for joining us in place of Dr. Crawford this morning.

Dr. Orenstein, I would like to ask you about the low prices of vaccines. There are several factors that affect the market for vaccines and influence whether manufacturers want to enter or even remain in the market. One of those factors is the price that is paid for the vaccines.

We welcome you, Dr. Crawford.

Dr. CRAWFORD. Thank you very much indeed.

Senator CARNAHAN. We have already introduced you and we were glad you were able to join us.

Dr. CRAWFORD. Thank you very much.

Senator CARNAHAN. One of the factors, as I said, is the price for the vaccines. The Federal Government purchases over one-half of our country's vaccines through the Vaccines for Children Program. The prices have not increased substantially since the program was implemented.

In Dr. Crawford's written statement, he makes this comment, that "Although the manufacture of biologic products is complex and demanding, and the need to update and maintain modern facilities is costly, the current prices paid for many vaccines are low compared with the prices of many other drugs." Could you comment on this and whether CDC or HHS has examined this in your discussions on how to alleviate future shortages?

Dr. ORENSTEIN. I think there has been substantial concern that vaccines are undervalued. In the past, vaccines had to pass a more rigorous test than most other products. That is, they needed to be cost-saving to society.

However, I think the issue of vaccine prices cannot fully explain the problems we are seeing today. For example, there is an inverse correlation between vaccines that we are having supply problems with and price. We are having more problems with the higher-priced vaccines than we are with the lower-priced vaccines at the moment. Another example is influenza vaccine, which there is very little public sector purchase, and for that price is the lowest of all of the vaccines, at about $7.

I think, in part, it deals with a society value issue, and as Mr. Pisano said, these are complex products, and I think the concern we have is the vulnerabilities, because in order to continue keeping up with good manufacturing practices, updating plants, making sure that all of the vaccines, including the older vaccines, have state-of-the-art technology supplied to them requires investments. And so I think economic incentives are going to be a key factor in trying to assure we have a long-term viable vaccine industry.

Senator CARNAHAN. Thank you. We will back up at this time and hear from Dr. Crawford, give him an opportunity to make his opening statement before we proceed.

TESTIMONY OF LESTER M. CRAWFORD, D.V.M., PH.D.,[1] DEPUTY COMMISSIONER, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. CRAWFORD. Thank you very much. I appreciate your gracious granting of me this time. I appreciate it very much, indeed. I am Dr. Lester Crawford, Deputy Commissioner of the Food and Drug Administration. Thank you for the opportunity to testify today.

I appreciate the Committee's interest in the current shortage of childhood vaccines and welcome the opportunity to participate in this hearing. FDA is concerned about the fragility of the Nation's vaccine supply and is committed to the availability of safe and effective vaccines. FDA-licensed vaccines have been protecting our Nation's children from deadly infectious diseases for almost 100 years. In fact, immunizations represent one of the most significant public health achievements of the 20th Century. Vaccines can be credited with saving more lives and preventing more illnesses than any medical treatment. Without question, continuing to ensure the availability of safe and effective vaccines is critical to protect the public health and prevent disease outbreaks.

FDA's regulation of vaccine manufacturing is essential to maintaining public confidence in U.S.-licensed vaccines. The importance of public confidence must be stressed. No other single health intervention has had the impact on disease prevention and our Nation's health as immunization with U.S.-licensed vaccines. For this reason, FDA carefully evaluates each licensing and regulatory action, balancing the importance of product availability while working with manufacturers to help assure that products are as safe as current technologies will allow.

Vaccines are different from most drugs in several respects, and achieving the highest quality in manufacturing is especially challenging and critical. First, they are most often produced from or use living cells and organisms as well as complex growth materials derived from living sources. Thus, the potential for contamination is higher than from most drugs, so the quality and purity of all source materials must be carefully monitored.

Second, the production of most preventative vaccines requires growing the immunizing agent in the production facility and the subsequent purification of complex molecules from these organisms. Growth conditions are complex. Subtle changes in materials and in the process itself or in conditions, such as temperature, can result in changes in the final vaccine that can affect its safety, its effectiveness, or both.

Third, the final vaccine itself is usually not, like most drugs, a simple molecule that can be tested for its purity and potency using simple chemical and physical methods. Instead, each lot of vaccines must be carefully tested for its composition and potency through the lot release process.

Finally, unlike most drugs which are given to people to treat an illness, vaccines are administered to large numbers of healthy people to prevent infectious diseases. For this reason, even very rare adverse events are generally not viewed as acceptable to healthy children and adults.

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[1] The prepared statement of Dr. Crawford appears in the Appendix on page 69.

Vaccine shortages can stem from a number of causes and the more recent shortages are not due to any single factor. In fact, the recent shortages stem from a number of factors, including the withdrawal from the market of one manufacturer, difficulties in manufacturing processes, temporary shutdowns of facilities for upgrades or maintenance or to correct manufacturing deficiencies, other factors, such as transition to thimerosal-free vaccine formulations.

When FDA inspects a vaccine manufacturer and finds deficiencies, the agency carefully considers the impact on product availability before taking action. In some situations, the agency may determine, after balancing all factors, that a decrease in the availability of a medically-necessary product could pose a substantial risk to patients. In such cases, FDA regulatory action may allow manufacturing of the critical product to continue, provided that certain conditions are established to ensure product safety.

The agency evaluates each circumstance on its own facts, balancing the medical need for the product against the safety assurances in place before a product is released for use. Whenever possible, FDA informs manufacturers of potential shortages to allow them to reallocate product to those who need it most and to take action to increase product inventory. In addition, FDA works with manufacturers that want to correct manufacturing deficiencies in order to avoid shortages of critical products. FDA works proactively and interactively with manufacturers to arrest shortage issues.

However, FDA does not have the authority to require manufacturers to stay in the market and produce a given vaccine, nor does FDA have the authority to direct manufacturers to increase production when a shortage occurs.

Thank you. I am happy to follow up with your questions or whatever else you would have me do. Thank you.

Senator CARNAHAN. Thank you very much.

Dr. Orenstein, I would like to get your comment on the issue of companies withdrawing from the market, an issue that I brought up with Mr. Pisano just moments ago. Would you comment on whether a shortage could be avoided if the government and other manufacturers were given advance notice and would you discuss how you would propose this matter to be addressed? In your experience, how far in advance can a manufacturer identify potential problems with the supply and when is the government usually notified by a manufacturer?

Dr. ORENSTEIN. I think in terms of trying to deal with your questions, I think if we could get advance notice, I think it would certainly help. I cannot say it would avoid all shortages, but it certainly could mitigate them.

For example, if we had known that one company was dropping out of the Td vaccine production well in advance, we could have alerted that other company. It would be nice to get at least 12 months' notice, because it takes about 12 months, for example, to produce a dose of tetanus diphtheria toxoids. If we could be notified and could share that information with the other companies, I think that would be a substantial benefit.

In terms of the issues about how long, the longer the better. What has happened in the past, as in the recent past, we have not had much advance notice when companies have left and we would

hope we would get that notice in the future for a company that is voluntarily leaving.

As Mr. Pisano said, Aventis Pasteur did present at a National Vaccine Advisory Committee workshop in February that they would pledge to give us substantial voluntary notification should they leave the market, and we would like to see the other manufacturers follow suit.

Senator CARNAHAN. Thank you. Dr. Crawford, I realize that safety is a No. 1 priority for vaccines, as it should be. Right now, we have several single source suppliers of vaccines. In your testimony, you mentioned that when you make a recommendation to a company to upgrade its facilities and it will affect production, you take into account the impact on supply.

But I have heard from some vaccine manufacturers who have expressed frustration that this is not always the case. They have concerns about how FDA is interpreting the current good manufacturing practices. Specifically, they are concerned in situations where there is not a safety concern that FDA is not taking into account the effects on supply when making a recommendation for upgrading their facilities.

Could you address this concern and expand on what criteria you use to make these decisions? In addition, would you comment on whether FDA tracks the impact of its regulatory decisions on the supply of a particular vaccine.

Dr. CRAWFORD. Yes. As you well know, the productive tension between the regulator, in our case, FDA, and the regulated is always somewhat tenuous. Vaccines, though, are a special product category that FDA regulates. We realize the effect not only on the public health in general, but in children's health in particular, so we try very hard to take into account all of these considerations.

Just a very few years ago, we had three times as many vaccine manufacturers as we do today, so we recognize this as a precious commodity and one that we have to do everything we can in our power to, first of all, assure that the vaccines are safe and effective, but second, to be sure that we still have manufacturers that are producing the vaccines that we absolutely have to have, and hopefully that these manufacturers will be in this country producing these vaccines.

So what we do when a decision has to be reached, either on the volition of the company or at the behest of FDA, is we offer what might be called technical assistance or technical service to those manufacturers to help them meet the requirements. Sometimes, a manufacturer will make a business decision to get out of the vaccine business or to stop manufacturing a certain vaccine and we try very hard, indeed, to make sure that we do not create some bureaucratic entanglement that makes that decision easy and not based on public health.

The criticism that has been voiced abroad about good manufacturing practices, not just in this area but across all of FDA, is that the good manufacturing practices presuppose that if a company is in conformity with these so-called GMPs, that the product then will be inherently safe and effective. Some companies and also some experts in the field are beginning to raise questions about whether or not the premise upon which GMPs are based is always correct.

We have heard those criticisms and we are examining GMPs not just in vaccines but in drugs and foods and the other areas we regulate to see if we do not need an overall reform of this particular means of regulation. FDA must stand four-square. In fact, our only real statutory role is to be sure that the vaccines are safe and that they are capable of immunizing America's children and others, and that is what we must stick to.

But in carrying out that function, we have to be absolutely certain that the means, mechanisms, and processes that we use to accomplish that are consonant with the latest research findings and that we are up to date with methodology that is being used in other countries and in other groups of countries. To that end, I can tell you that we have not only heard them, but we are seriously looking at GMPs as a means for accomplishing your statutory mission and I would hope, as everything can be improved, that we will improve these over the next couple of years.

Senator CARNAHAN. One final question—I thank you, Dr. Crawford, and then we will turn the questioning over to Senator Bunning.

I would like for both of you, if you would, to address the government's plan to deal with future shortages. As I have already stated, I am concerned about the underlying factors that have contributed to this shortage and the fear that they will remain even after the current shortage is alleviated. What are CDC and FDA doing to find long-term solutions to prevent future childhood vaccine shortages and what are your proposals on how to achieve those goals?

Dr. ORENSTEIN. The National Vaccine Advisory Committee has been looking at five areas for long-term changes. One deals with economic incentives and the need to assure a viable vaccine industry. A second deals with streamlining of the regulatory process. A third deals with government supported vaccination. A fourth deals with stockpiles. And a fifth deals with liability.

We are looking forward to their final report as well as the report from the General Accounting Office, and when those come, we will be looking at what those recommendations are and determining which of those areas we need to take action in. One of the ones that we have certainly used in the past that has been helpful have been stockpiles as a way of dealing with year-to-year changes in production. As Mr. Pisano mentioned, production disruptions will happen. In the past, we have had stockpiles that have taken care of them. We did not have stockpiles for many of the vaccines in shortage today, and those are some of the issues we will be evaluating.

Senator CARNAHAN. Thank you.

Dr. CRAWFORD. Yes. Within the Department of Health and Human Services family, the Food and Drug Administration has the lead in the integrity and availability of the vaccine supply. We cooperate closely and intimately with CDC and also to do the job of regulation that the statutes and also the national public health requires.

So the productive cooperation between us and CDC continues. We are very sensitive to whatever we can do to improve availability and effectiveness of vaccines. We cooperate with CDC and that cooperation is willing and, hopefully, productive.

Senator CARNAHAN. Thank you. Senator Bunning.

Senator BUNNING. Thank you, Madam Chairman.

This can be answered by either or both. Are there some areas of the country more affected by the vaccine shortage than others, and if so, why?

Dr. ORENSTEIN. The shortages are spotty and it depends on the distribution systems. It is not like there is one uniform national distribution system. So as you heard from the earlier testimony, different doctors may have different shortages for different vaccines.

The Federal Government purchases about 52 percent, on average, of the vaccines and distributes them to the States, but the other 48 percent is in the private sector and it will vary.

For four of the five vaccines, the distribution appears to be fairly equal between public and private sectors. The biggest problem in the public sector, or disproportionate factor affecting public clinics has been the DTaP vaccine, and that is because one of the companies that had very limited supplies chose to focus that supply into the private sector. Hopefully, all of that will be relieved with the licensure of the new vaccine.

Senator BUNNING. Dr. Crawford, do you have anything to add?

Dr. CRAWFORD. I have nothing to add.

Senator BUNNING. Do either of you have an estimate on how many children are not receiving the necessary vaccine at the proper time because of the shortage?

Dr. ORENSTEIN. That is a question we would like to have an answer for, but we do not. We measure—we will, in my opinion, see decreases in immunization coverage, but part of the problem is when we measure that coverage. The immunization series can begin as early as birth, but the basic series tends to be completed by 18 months of age, so we begin our measurements at 19 months of age. So many of the kids who are currently impacted by this shortage have not yet entered our measurement system.

We do have data from the Commonwealth of Puerto Rico, where, because of their problems in gaining access to the DTaP vaccine, they made a decision to defer the fourth dose of DTaP, and what happened is their coverage dropped from the mid-90's to the mid-30's as a result of that. Now, their DTaP–3 coverage is still very high. This is action they took to try to mitigate the results of the shortage. So we have some data there that are really concerning and we will have to see what happens in the other States as children age into our system.

We are also monitoring disease and we have not seen, as yet, outbreaks of disease as a result of these shortages, but certainly we remain very concerned.

Senator BUNNING. Dr. Crawford.

Dr. CRAWFORD. Just one little thing to add. We would be prepared to use various interpretations of our law to help with these spotty shortages that might develop because no one wants to see vaccine schedules be disrupted and children not being able to be vaccinated on time and maybe disruptions in the school system.

We have a process called the Investigational New Drug Process where if a certain kind of vaccine is approved in another country, for example, and CDC sends us a signal that this might help ame-

liorate some of these problems, we are certainly willing to invoke that. It is not used for that normally because it actually was created by Congress as a means to develop the investigational aspects of vaccine production, but we certainly want to send a signal here that we are willing to be as creative as we can be about helping with these shortages and also applaud CDC's work in this regard. We would be interested in the figures that are accumulated.

Senator BUNNING. Since the earlier testimony from others said that sometimes there is only one manufacturer maintaining a certain vaccine, has the CDC or whoever, the FDA, looked to foreign sources, foreign supplies? Are there not other foreign companies making the same vaccines?

Dr. CRAWFORD. CDC would probably have a better fix on this than we do, but our understanding is that in other countries, although there might not be shortages, generally, just enough is produced in order to meet their own supply and demand.

Senator BUNNING. The reason I bring that up is that HHS, when we are looking at the war against terrorism and the potential of a smallpox problem, looked to foreign sources to manufacture enough of that so that we could have a supply to fit the population.

Dr. CRAWFORD. Absolutely.

Senator BUNNING. I am looking at other types of children diseases.

Dr. ORENSTEIN. Two of the four manufactures that produce for the U.S. market have their headquarters actually abroad. One of the major suppliers, Glaxo Smith Kline, has helped for several of the vaccines I did not mention today, because even though there are some production disruptions, they have been able to cover the gaps.

There is a problem when you bring in an investigational vaccine to be used in a routine program, an "experimental" vaccine, even if it is used and approved abroad. We have had problems with trust, as you have mentioned earlier, and so using an investigational vaccine, particularly if there is some of the approved vaccine, is problematic for——

Senator BUNNING. In other words, you tend not to bring one that we have not had tested here in the United States?

Dr. ORENSTEIN. Exactly. What I think we need to do is, are there ways of facilitating other companies coming and getting their vaccines licensed——

Senator BUNNING. That was one of my questions, about how long the FDA takes to approve a vaccine, or for that matter, if we went outside the United States, for a foreign vaccine for children to be approved.

Dr. CRAWFORD. We take a shorter amount of time on vaccines, particularly given the current situation, than virtually any other thing we regulate, including food additives, for example. We are very sensitive to developing companies. With them, we have to work with them from the earliest onset to make sure their facilities are capable of producing safe and effective vaccines within the time table. So the sooner we can get with them as they are beginning to enter the market, the better it is, and we are available for that. I want the word to go forth that we will provide consultation with them, meet with them at their behest, and also help as far as we

can within the meaning of the law to provide the technical assistance that is needed.

Senator BUNNING. Last, Mr. Orenstein, on the first panel, Mr. Pisano mentioned that industry representatives are no longer fully permitted to participate in CDC's working groups. Why is that?

Dr. ORENSTEIN. First of all, the Pharmaceutical Research and Manufacturing Association is a liaison member to our Advisory Committee, so they are able to make comments and participate in the full deliberations of the Committee.

Senator BUNNING. I understand the comments, but the working groups——

Dr. ORENSTEIN. I think the major issue on the working groups has been concern about perceptions of conflict of interest. These tend to be small meetings. They tend to be closed. The manufacturers can now be invited, and are usually invited, to present and discuss and answer questions for them. They are not there for the deliberative process, because as Mr. Pisano mentioned, there is a conflict of interest with regard to how vaccine recommendations are made.

Certainly, I think we have all learned from the thimerosal episode and others that manufacturers have a very valuable information base that is critical to adequate policy making. The goal is to have them present that information, but not be there during the actual deliberations.

Senator BUNNING. Would it not help, though? Would they not have the availability to tell you if they were going to stop manufacturing like you would like to have a year ahead of time, or would it not be better if there was a hands-off but a close relationship so that you would know? In other words, if they are not going to manufacture a given childhood vaccination or vaccine, that you would know it up front?

Dr. ORENSTEIN. I think we certainly would like to know it up front. I am not sure the working group actually is the place. I think that would be a one-on-one relationship between us and the companies, I think, that is what we have done, and we did that with influenza, where each of the companies provided confidential proprietary information to us and then we were able to aggregate it and share it.

I think the issue on the working groups is differentiating provision of information, where I think the manufacturers are absolutely critical, and the actual deliberation decisionmaking process, and that is what we have tried to do, is to keep the information side flowing, but when deliberations take place, to limit that.

Senator BUNNING. Is it both of your opinions that the critical shortage, except for one vaccine, will be over by the end of this summer and probably all of the critical five will be over sometime in 2003?

Dr. ORENSTEIN. Based on the projections we have gotten from the vaccine industry, yes.

Dr. CRAWFORD. I agree.

Senator BUNNING. Thank you very much, Madam Chairman.

Senator CARNAHAN. Thank you, Senator Bunning, and I certainly thank all of those who have testified today. I also want to thank Dr. Goodman for his willingness to stand in for us here at the last

minute. Your written statements and your oral testimony and your responses to the questions have been very helpful.

As we have seen today, this is a very complicated issue. The shortage of childhood vaccines has been caused by many different factors, so there is no "quick fix." But by highlighting this situation today, I hope that we have moved a step further to finding a solution. We need to continue to keep the spotlight on this issue. Communications is key here, and by joining together to talk about the issue, we are participating in a process that will ultimately lead to a system that will work better to prevent vaccine shortages from occurring. We need to continue the national dialogue until the underlying problems that have contributed to the shortage are addressed. It is important for all of our children's health and their future.

Once again, I would like to thank all of our witnesses for participating in the discussion. I also extend my thanks to the physicians and others in Missouri who helped us prepare for the hearing, some of whom have submitted written testimony. I ask that the testimony of Dr. Robert Hoffman from St. Louis and Harold Bengsch, Director of the Springfield-Greene County Health Department, be entered into the official record.[1]

We will keep the record of this hearing open for 1 week in case the witnesses would like to submit any additional comments or if other Members would like to submit any questions to you in writing.

Thank you very much. This hearing is adjourned.

[Whereupon, at 11:23 a.m., the Committee was adjourned.]

[1] The prepared statements of Drs. Hoffman and Bengsch appear in the Appendix on pages 83 and 85 respectively.

APPENDIX

American Academy of Pediatrics

TESTIMONY

BEFORE THE

UNITED STATES SENATE

COMMITTEE ON GOVERNMENTAL AFFAIRS

"PROTECTING OUR KIDS: WHAT IS CAUSING THE CURRENT CHILDHOOD VACCINE SHORTAGE?"

PRESENTED BY:
TIMOTHY F. DORAN, MD, FAAP
CHAIRMAN OF PEDIATRICS
GREATER BALTIMORE MEDICAL CENTER

June 12, 2002
9:30 a.m.

Department of Federal Affairs
The Homer Building
601 Thirteenth Street, N.W.
Suite 400 North
Washington, D.C. 20005
202-347-8600 / 800-336-5475 / FAX: 202-393-6137

Good morning, Madam Chairwoman, members of the Committee, I am Dr. Tim Doran, a practicing pediatrician who has taken care of children for almost 20 years. I am also Chairman of Pediatrics at the Greater Baltimore Medical Center, a community hospital in Baltimore, Maryland. On behalf of the American Academy of Pediatrics, I would like to thank you for the opportunity to testify today about the current shortage in childhood vaccines.

The American Academy of Pediatrics (AAP) is an organization of 55,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents and young adults. My testimony today reflects not only my experiences from my pediatric practice but also those of colleagues from across the United States. As a practicing pediatrician, I would like to share with you my perspective on the current vaccine shortage, discuss the consequences this has had on vaccine delivery to my patients and their parents, and the impact on my practice.

Overview:

As primary care pediatricians, prevention of disease through immunization is a priority. It is an integral component and major goal of the comprehensive pediatric health care we provide to infants, children, adolescents and young adults. Overall, we deliver approximately 75% of all immunizations. The predictable delivery of safe and effective vaccines is central to our goal of disease prevention.

Immunization is one of the greatest public health achievements of the 20th century and has saved millions of lives. Since the widespread use of vaccines, millions of children have avoided terrible diseases that can cause great suffering and in some cases, death. For example before immunization, polio paralyzed 10,000 - 25,000 children and adults, rubella (German measles) caused birth defects and mental retardation in as many as 20,000 newborns, and measles infected millions of children, killing 400 - 500 and leaving thousands with serious brain damage. Immunizations have reduced by more than 95 to 99 percent the vaccine-preventable infectious diseases in this country.

In the last decade a number of positive changes have occurred in the delivery of vaccines to infants, children and adolescents. Now, in addition to diphtheria and tetanus toxoids and acellular pertussis (DTaP), polio, measles, mumps, rubella (MMR), and Haemophilus influenza type b (Hib), several new vaccines have been added to the routine vaccination schedule for children, including the hepatitis B vaccine (added in 1994), varicella (chicken pox – introduced in 1995), and the pneumococcal conjugate vaccine (added in 2000).

However, recently, there have been some less-positive changes. In my 22 years of practicing pediatrics, including my pediatric residency training, I have never witnessed a vaccine shortage such as we see today. My colleagues and the parents of my patients are alarmed about the current situation. The recent disruptions and shortages – remarkable for both the number of different vaccines involved as well as the scarcity of the available supply – have been a wake-up call to the average practicing pediatrician as we come to the realization that the vaccine supply, and perhaps the overall vaccine system, is far more fragile than we had imagined.

Pediatric Practices:

My office experience has been that the distribution of the required childhood vaccines is spotty and unpredictable. In recent months, my practice has seen shortages in several vaccines. These shortages reflect the national disruption of routinely administered vaccines against the eight out of 11 vaccine-preventable childhood infectious diseases. The problem is particularly acute with the new 7-valent pneumococcal conjugate vaccine (PCV7, Prevnar). This vaccine helps protect children from life-threatening meningitis (an infection of the covering of the brain) and blood infections. Many of my pediatric colleagues, such as those in Wisconsin, are completely out of this vaccine. According to a pediatrician from New Mexico, his high-risk patient population of American Indian/Alaskan Native infants currently has no supply of PCV7. This is especially troublesome because he recently diagnosed a four-month old Navajo infant with a case of pneumococcal meningitis - a vaccine-preventable childhood infectious disease. Also in short supply nationally is the tetanus-diphtheria toxoids (Td) vaccine. Td has been in

limited supply for over a year now. This has affected the ability to give teens the booster Td they need. Other vaccines in short supply include DTaP, varicella, and MMR.

A pediatrician in St. Charles, Missouri recently called the offices of the American Academy of Pediatrics to describe his serious vaccine shortage problem. He has a small private practice - two pediatricians and one nurse practitioner. He has had difficulty since last September in obtaining both the Prevnar and varicella vaccines. Currently he does not have a supply of either vaccine. Imagine his dismay when he was advised by a patient's mother, who arrived with her son for his one year well-child visit, that she believed her son had been exposed to chicken pox. If he had any varicella vaccine to offer the patient, research data has found that the child's disease could be ameliorated by vaccination.

As you have heard from the CDC representative, several factors are contributing to the fragile supply in this country. Many vaccine manufacturers are facing increased profitability challenges that force them to re-think their place in the market. For example, the U.S. Food and Drug Administration's Good Manufacturing Practices are being enforced more stringently, which, in some cases, will mean that vaccine makers must build new plants to be in compliance. Some manufacturers have decided it's not worth the investment and have dropped out of the market. For others, poor demand – and thus, poor sales – has been too difficult to surmount, as was the case with the recent withdrawal from the market of the Lyme vaccine by Smith-Kline-Beecham.

Also contributing to the shortages are production issues (including unexpected demand for a vaccine that exceeded supply), decreased yields of the biologic materials used in certain vaccines, the elimination of some vaccines containing thimerosal as a preservative, and insufficient vaccine stockpiles.

At times I have had to explore alternative ways to obtain the full supply of vaccines my practice needs. Sometimes I have been more successful obtaining vaccines directly from pharmaceutical representatives than through the bulk purchasing mechanism through the

hospital pharmacy. At other times, I borrowed from other practices. There was no opportunity to plan in any reasonable way to anticipate the supply, and unfortunately the pharmaceutical representatives are of little help in predicting when depleted vaccines will become available.

Impact and Consequences:

The real-life impact of these shortages can not be denied. An estimated 11,000 babies are born each day in the United States, each requiring 20 doses of vaccine by age 18 months to be protected against 11 childhood diseases. In addition, there are booster vaccines, such as Td, given in adolescence. A vaccine shortage quickly impacts thousands of families every day.

The parents of my patients have been understandably anxious when they learn that a vaccine is unavailable. They know that there is a small but finite chance that their child might become ill with an otherwise easily-preventable disease because of a delayed or altogether missed vaccine. And many of these diseases, such as measles and meningitis, can be devastating – even fatal – in young children.

Because of recent media publicity and campaigns by anti-vaccine groups, I spend a significant amount of time with many parents reassuring them that our vaccines are safe and beneficial. I cannot help but wonder how my credibility, and that of my colleagues, suffers when I then have to explain that these important and safe vaccines are not available for their young child, now at risk for contracting a life-threatening illness. This unduly disrupts the confidence between doctor and parent - a trust that is fundamental to the parent - pediatrician relationship.

Additionally, children who are not vaccinated could possibly be denied entry to school or access to day care. How will school systems deal with increasing numbers of school-age children registering without having completed the vaccination requirements? What will struggling working parents do if their care provider bars their child from day care because he or she is behind on vaccinations? Moreover, what will parents do when children

become unnecessarily sick with vaccine-preventable illnesses that prevent them from attending school or day care and parents miss days from work to care for their sick child?

Along with the stress on the vaccine delivery system and on parents and patients, the vaccine shortage has an administrative impact on my practice as well. We must now create a system of call - back lists and tickler files to reach those most in need of missed vaccines when they become available. My experience and that of other pediatricians has been that these systems are not very reliable or effective. Even in a relatively affluent population, the level of compliance with these call-backs is only fair. The need to effectively track patients and get them back in the office to receive vaccines adds a heavy administrative burden on practices that are already overwhelmed with complex billing issues, referrals, insurance verifications, coding, school and camp forms, medication permissions from schools, prescription refills, phone calls from sick patients, inventory controls, OSHA compliance and documentation, and prolonged holds on the telephone for insurance approvals for certain drugs and procedures.

All this is occurring at a time when the Centers for Medicare and Medicaid Services (CMS) has failed to recognize the physician work associated with the provision of vaccines to patients. This will result in inadequate payment for these services, which will further exacerbate and threaten the already fragile vaccine delivery system. Such lower payments create a disincentive for a pediatrician and other doctors to administer childhood immunizations in a child's "medical home."

Conclusion:

As you can see, the fragility of this nation's vaccine supply is a broad, complex problem, and its solution can only come from the strong leadership and the close involvement of all stakeholders. I believe it is crucial to our children's health that we continue to work towards ending the current shortage as well as look for solutions to avoid future disruptions in supply. I am grateful to have been here today to share my perspective as a practicing pediatrician.

Thank you.

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Testimony for hearing before the Committee on Governmental Affairs
"Protecting our Kids: What is Causing the Current Shortage in Childhood Vaccines?"
June 12, 2002

Mr. Chairman and distinguished members of the Subcommittee:

I am Dr. Mary Anne Jackson, Professor of Pediatrics and Chief of the section of Pediatric Infectious Diseases at Children's Mercy Hospital and Clinics in Kansas City, Missouri, an area of 1.78 million people. Our pediatric center provides comprehensive primary and tertiary specialty care in 35 pediatric subspecialty areas to children from a 140 county region in Missouri and Kansas plus adjacent portions of Nebraska and Oklahoma. It is the only pediatric medical center between St. Louis and Denver and over 300,000 outpatients and 11,000 inpatients are treated annually.

As a specialist in pediatric infectious disease, I have 3 major roles: clinician, researcher, and educator. I am a clinician providing care and consultation for children with infections. Many of the children for whom I provide care are generally otherwise healthy children, hospitalized with infections such as pneumonia, meningitis, bone infection, or Rocky Mountain Spotted Fever. Children with AIDS, cancer, or transplanted organs develop infections that are highly unusual owing to the failure of their immune system. Premature infants, patients in our burn unit, or patients with complex underlying disease often develop infections that provide special challenges. In my second role, I am a clinical researcher and have presented data nationally that focuses on issues of emerging infections, antibiotic resistance, and prevention of communicable diseases.

I think my most important role, though, is as an advocate and educator for children's health issues. As such, I teach medical students and pediatric residents and provide consultation to community primary care providers. As a community resource, my colleagues and I speak formally to groups of physicians locally, regionally, and nationally. On a daily basis, community pediatricians call us with specific questions related to patients who present diagnostic dilemmas or general questions regarding community outbreaks of disease, antibiotic resistance issues, and such. Last fall, for instance, we provided verbal and written materials to our community physicians regarding smallpox and anthrax. Questions regarding communicable disease and immunizations routinely account for ten to 25 percent of such calls.

The American Academy of Pediatrics Committee on Infectious Diseases offers a handbook to the pediatric practitioner known as "The Red Book". This book summarizes recommendations for childhood immunizations as well as addressing the care of children with a variety of infectious diseases. In the 25th edition, the editors note "the ultimate goal of immunization is eradication of disease; the immediate goal is prevention of disease in individuals or groups. To accomplish these goals, physicians must maintain timely immunization as a high priority in the care of infants, children, adolescents, and adults." I think the key words that bear emphasizing are immunizations must be timely and are of the highest priority. The global eradication of smallpox in 1977 and elimination of polio from the Americas in 1994 are offered as models for control of disease through immunization. There is no doubt that these accomplishments were achieved by combining an effective immunization program with intensive surveillance and effective public health control measures. In addition to polio and smallpox, immunization has successfully curtailed or almost eliminated diphtheria, measles, mumps, polio, rubella, tetanus, and Haemophilus influenzae type b disease.

When I was a pediatric resident at Cincinnati Children's Hospital Medical Center in the early 80s, we routinely treated infants with Haemophilus influenzae type b meningitis; 5% would die and 15% suffered sequelae (complications) from infection, most commonly deafness. Since 1993, following the implementation of conjugate Hib vaccine, I have seen no cases of this disease which previously was so common that a week didn't go by that an affected child wasn't admitted and treated in our institution and pediatric institutions throughout the country. Chickenpox, which is generally regarded as a benign and inevitable infection of childhood, annually caused 4 million cases, 11,000 hospitalizations, and 100 deaths prior to implementation of vaccine in 1995. In our institution, complications of chickenpox, including toxic shock syndrome, were encountered commonly in the late 1980's and early '90s and are infrequently seen today.

However, because the pathogens responsible for these diseases persist in the US and in other countries, immunizations need to be continued and our program is fragile at best. In the US, only 80% of children are adequately immunized; in the state of Missouri, that rate is 84%. In the Kansas City area, efforts from organizations such as the Partnership for Children and the Mid-America Immunization Coalition have worked tirelessly and the percent of children fully immunized has risen from 52% in 1990 (the national average being 40-60%) to 85% in the year 2000 (national average 79%). There are disparities in our regional counties though with a low of 66% in one Kansas county and a high of 94% in one Missouri county. Yet, we can not become complacent as we continue to see children with vaccine preventable diseases. Since 1984, when I came to Children's Mercy, we have cared for 341 infants and children with pertussis (whooping cough) including a two-month-old child who recently spent a month in our intensive care unit. In my community, within the last year or so, an infant from Independence, Missouri died of complications from chickenpox; on November 12, 2000, a five-month-old old boy died of pneumococcal meningitis; and on May 20, 2001, a sweet 15-year-old boy died of liver cancer, a complication of hepatitis b infection inadvertently transmitted to him at birth. These were all deaths due to vaccine preventable diseases.

An unprecedented and unanticipated shortage of routinely recommended vaccines has resulted in inadequate supplies of eight of the eleven routinely administered vaccines, with shortages more acute in the public sector than in the private sector for many of these vaccines. In our state, the Vaccine for Children program supplies vaccines for approximately half of children; at our institution we see 50,000 children for well-baby care, virtually all of them receiving vaccines through the public sector. While the state of Missouri has worked hard to ensure that available vaccine is equitably distributed, we have all had to change our immunization practices dealing with the shortage that most drastically affected supplies of Td vaccine, varicella vaccine, and, most recently, pneumococcal conjugate vaccine (we currently have none). Our physicians are vigilant about keeping track of a child's immunization status. A computer-generated list of each child's immunizations is placed on the front of his or her chart at every visit. Similarly, in private practices the child's immunizations are listed, usually, in the front of the chart. We strongly advocate that opportunities to immunize are not missed.

The vaccine shortage has impacted the physician's ability to provide a consistent recommendation and practice for vaccine implementation. At our institution and in the community, in the event a vaccine is not available, a written list is kept and children are called back once a supply of vaccine comes in. While the CDC has recommended prioritization of vaccines, my opinion is that this is often not followed. In some practices, there was a sudden vaccine shortage such that prioritization could not occur. Other practices said simply that it is impractical to triage vaccines in the course of pediatric practice. Whether or not a child returns for vaccines once notified is unknown.

The vaccine shortage has impacted on our state's immunization requirements. The state of Missouri has altered its recommendation for day care center attendance, telling physicians in July of 2001 that varicella vaccine was mandated and, less than a year later, rescinding this recommendation in light of vaccine shortages.

What is the impact of vaccine shortages? National data suggest that delays were of sufficient magnitude to have a negative impact on immunization coverage with a decline of almost 10% from 1999 to 2000. While in our state, this decline appears smaller (2%), there is no question that a fall below 80% (and we are tenuously close to this margin) may result in an increase in cases of disease. Data from 2001 will likely show further declines.

Children who start their vaccines on time are clearly more likely to stay current throughout their first year. I am currently involved in an educational program to improve immunization rates in our community and, especially, to empower parents to insist that their child be immunized on time. This appears near impossible to implement if the vaccines are not there to give. Our message to the public and professionals becomes muddled when we document the scope of disease that can be prevented by immunization and then delay and defer opportunities.

Prevention of infectious diseases by immunization has been one of the great public health achievements of the twentieth century. Whether our current vaccine shortages are caused by companies leaving the vaccine market, manufacturing and productions problems, or insufficient stockpiles, it is clear that one of the indelible marks of these shortages is that parents and professionals are confused and frustrated and all strides made in the last decade may go by the wayside. Our goal should be to maintain a supply of licensed vaccines that are safe and effective. These vaccines should be available for every child and adult in the US. Vaccine research, development, and production must be enhanced. And last but not least, educational efforts will need to be intensified to ensure that our children are healthy now and as we face the challenges of the future.

Statement PhRMA

WAYNE PISANO
EXECUTIVE VICE PRESIDENT
AVENTIS PASTEUR NORTH AMERICA

FOR THE
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA

BEFORE THE
GOVERNMENTAL AFFAIRS COMMITTEE

OF THE

UNITED STATES SENATE

June 12, 2002

Good morning. On behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA), I am pleased to appear at this hearing today on childhood vaccines. I am Wayne Pisano, Executive Vice President of Aventis Pasteur North America. PhRMA represents the country's major research-based pharmaceutical and biotechnology companies, including the four PhRMA companies that make 100% of children's vaccines, and 90% of all vaccines. Many people are surprised that the industry is so small, but that fact is largely the result of the liability crisis of the 1980's that drove most companies out of the market. I will talk more on this later in my testimony.

We are all keenly aware of the vaccine shortages facing our nation today. Although most of these shortages will be resolved in 2002, this hearing provides an excellent forum for understanding the underlying causes as well as addressing what can be done to minimize the chances of recurrences and how best to act if there are recurrences. The fact that the private sector has the capacity to respond reasonably quickly to supply issues demonstrates the strength and vitality of our industry. While we are addressing supply issues successfully, I will offer six specific suggestions as to how our nation's vaccine supply can be strengthened while maintaining a vital and productive industry.

Our nation benefits from the efforts of several world-class vaccine companies. At Aventis Pasteur, for example, vaccine production began at our Swiftwater, Pennsylvania site in 1897, with an immediate goal of providing an improved smallpox vaccine. More than a hundred years later, this campus continues to develop and manufacture improved and new vaccines to protect against a variety of diseases. Over the years, we've had some enormous successes, including the first application of conjugate vaccine technology and the first infant acellular pertussis vaccine. We have also invested enormous resources into vaccines that, for a variety of reasons, did not reach the marketplace.

Although these new product failures do not affect supply directly, the economics do impact the attractiveness of the industry. The full cost of development – contrasted with historical vaccine pricing – is at odds.

We have in the country a unique and amazing vaccine enterprise that has resulted in freedom from disease for millions of children. Many of today's parents have never heard of diseases such as polio, Hib or measles, outside of the context of the vaccines that prevent them. Many physicians would be treating some of the tens of thousands of cases of rubella, diphtheria, pertussis and other potential killers if not for our successful efforts. Smallpox has been eradicated. Wild poliovirus has been eliminated in the U.S. and many other countries with global eradications underway or being discussed. Diphtheria, rubella, tetanus, mumps measles – even Hib disease – are now rarely seen. Since the introduction of a vaccine for Hib a few short years ago, the incidence of this disease has plummeted 98 percent! Vaccines, in the hands of a robust, cooperative public and private health delivery system, have made these diseases historical artifacts.

This success story is not restricted to the millions of children who receive a vaccine each year. Adults also have benefited enormously from immunization. Nearly 80 million people received an influenza vaccine this season, nearly triple the number that did so a decade ago. While the flu vaccine's most important benefit is the number of lives it saves, it also has contributed to reduced incidence and severity of disease, and, as more healthy younger people opt for an annual shot, a payoff to employers in reduced absenteeism and healthcare costs as well.

With that as background, it is time to take a step back and consider how the immunization enterprise in the country works, what we are doing right and what might be improved.

There are several characteristics of the vaccine enterprise that make the close cooperation of all participants, within the bonds of the antitrust laws, critical for proper alignment of supply with demand.

First, unlike almost any other aspect of our healthcare system, vaccines protect our entire society in addition to improving personal health. So, there needs to be much closer collaboration during vaccine production, distribution and administration than for other healthcare interventions. Everyone participating in the immunization enterprise must be involved, be they manufacturers or physicians, nurses or public health workers, policy makers or managed care.

Second, whether or not a vaccine will ever be used widely – or at all -- will depend on recommendations formulated through extensive public discussion. That collaborative approach, accompanied by adequate timeframes, has moved mountains over the years.

Third, the regulatory approval process for new vaccines, and for changes to existing vaccines, is highly complex and lengthy with timetables that are difficult to

predict. Taking into consideration the fact that production schedules can run 12 months and longer, any abrupt changes in policies that can influence demand for a vaccine, or the unanticipated departure of a manufacturer, can result in supply interruptions that last for months.

Fourth, as I stated earlier, the liability crisis of the 1980's drove most vaccine manufacturers out of the market. Over a dozen vaccine companies existed in the early 1980's but liability problems shrunk that number to the four that exist today. In 1986, Congress created the Vaccine Injury Compensation Program, which helped alleviate some of the liability concerns. But the industry is once again facing the possibility of massive lawsuits and mounting legal bills, which we are convinced warrants shoring up the VICP.

For the most part, the immunization enterprise is quite efficient. Every child in the United States has access to immunization. No one needs to go without because of cost; both public and private sectors have honed programs over the years that get children to vaccines and vaccines to children. Nearly 20 million routine pediatric visits take place each year, often because immunization is the incentive.

Fifty years ago there were only four antigens available to children: smallpox, diphtheria, tetanus and pertussis. By the 1960's we had added polio, measles, mumps and rubella to the regimen; in the following decades Hib, hepatitis B, varicella and pneumococcus were included. Today, twelve diseases are largely prevented through the pediatric immunization series. We believe that we are still in the early stages of a remarkable era in disease prevention and that additional vaccines will be available during the next few years as current vaccine candidates progress through the pipeline. These new vaccines will either be new combinations allowing a greater number of antigens to be given in a single injection or entirely new vaccines to protect against diseases for which we have no vaccine today.

Yet, with what has become nearly universal access, tremendous coverage and added protection, there are still deficiencies in the system that require a tune-up.

During the past few years, we have had several vaccine shortages, mostly because of short-term acute reasons. Some, as in the case of flu vaccine, reflect the inherent difficulty in biologics manufacturing such as when the vaccine needs to be reformulated every year. There is always some degree of uncertainty and the solution lies with the vaccine enterprise that manages distribution and immunization policy. We need to look at what causes shortages, what exacerbates them and what might mitigate them. We have seen a confluence of factors over the past two years that has led to the recent shortages.

Nature of Vaccine Manufacturing

Let's look for a minute at the nature of vaccine manufacturing, which is complex and involves a number of variables that don't exist in pharmaceutical manufacturing. Vaccines require the use of biological organisms, viruses and bacteria, which will not

always grow or respond on demand. It is not a matter of opening a tap and pouring out vaccine, no matter who controls the tap. Production lead times are long and the quality control process is the strictest possible. Every lot must pass purity and potency testing not just by the manufacturer but by the FDA as well. As a result, supply and demand will be misaligned when policy changes increase demand before supply is available. We have experienced several such acute shortages during the past several years.

Discontinuation of Vaccine Production

The decision by manufacturers to discontinue production of certain vaccines has been the most significant factor in a series of serious but temporary shortages. In the last two years – after a period of relative stability – we have lost production of several vaccines. Companies may decide to leave marketplaces when a product no longer provides, in a particular company's assessment, a sufficient potential return on investment. Some of the factors that influence return on investment are cost of new product development, cost of manufacturing, product demand and the existence of free market pricing versus various forms of government price controls. When a manufacturer discontinues production, ramp up by other manufacturers to fill the gap may take more than a year for some products.

Tetanus Shortage 2001-2002

Tetanus vaccine is an example of an acute shortage that we anticipate resolving this year. Last year, there was an unanticipated withdrawal by a tetanus vaccine manufacturer leaving Aventis Pasteur as the only manufacturer of Td, DT and TT. Aventis Pasteur had taken a hard look at there own tetanus operations several years prior to this and decided to make the infrastructure upgrades necessary for this essential product. However, at the time we did so we expected that we would be supplying only part of the marketplace. Since it takes approximately 11 months to produce a batch of tetanus vaccine, it soon became evident that there would probably be a national shortage following the other company's exit. We immediately began working with the CDC to manage the available Td doses to ensure that all critical immunization needs were being met and that tracking of deferred booster doses was implemented. This shortage has resulted in some inconvenience, to be sure, but, because of strong collaboration between the manufacturer, the CDC and medical societies, we have succeeded in protecting the health of our citizens. We are implementing plans to return to a normal supply situation – in an orderly manner – by the end of the year.

Another critical consideration over the past year has been the maintenance of safety stocks of Td vaccine. No day underlined the need for a safety stock as did September 11th. Aventis Pasteur was able to deliver 50,000 doses of tetanus to New York City and 10,000 to New Jersey within hours. Similarly, we are prepared to respond to natural disasters that may place large, sudden demands for Td deliveries.

As an added precaution, Aventis Pasteur has just obtained American licensing for our Canadian DTaP product – Daptacel – which will ameliorate shortages of this important childhood vaccine.

Likewise, supplies of mmr vaccine have stabilized and varicella vaccine supplies are improving and providers may be able to return to the recommended vaccination schedule by August of this year.

Impact of policy changes and regulatory approvals

Policy and regulatory changes also have an enormous impact. I'd like to talk about the industry's experience with two ends of the spectrum and their implications to supply.

Thimerosal

Since mid-1999, policymakers have taken the position that Thimerosal must be removed as a preservative from all childhood vaccines.

The removal of thimerosal can serve as a valuable glimpse into the cascade of events that can – and did – exacerbate a shortage of a vital childhood vaccine, dtap, following the decision to remove thimerosal from the product.

Thimerosal serves as a preservative. It also allows healthcare providers to purchase and use convenient multi-dose vials without risking bacterial contamination as they continue to draw from a vial. Without thimerosal, single-dose packaging must be used. The decision to remove thimerosal significantly impacted supply. The manufacturing process itself had to be changed in order to assure the aseptic filling of the single-dose vials. In addition, the process changes lengthened the manufacturers' timelines and yields dropped significantly since it is necessary to overfill every vial to ensure that the provider can remove a full dose. The cumulative effect of this overfill is dramatically greater for single-dose vials than for multi-dose vials.

Reformulating a vaccine, as was required in order to convert from a preservative-containing vaccine to a preservative-fee vaccine, requires first completing passage through the regulatory approval process. Any change to a vaccine is a complex endeavor. Manufacturers must take the reformulated product through a license application, with concomitant establishment of new procedures, validation, testing, labeling and getting the product into the marketplace. The net effect is that we invested approximately two years' development effort to replace an existing product.

The removal of thimerosal presented significant and complex problems as we changed from a multi-dose to single-dose presentation. This change not only

took a considerable amount of time and effort, but also reduced our total output by approximately 25%. This is obviously a significant impact.

All vaccine manufacturers strive to supply safe and effective products. However, the point here is that actions have consequences and that those who make the rules need to carefully weigh credible evidence so as to avoid decisions based on unreliable data, and must factor in the implications of their decisions on supply and allow realistic time frames when considering such changes. Every independent action has dependent reactions, some of which are very detrimental.

CGMPs and Team Biologics

While the current Good Manufacturing Practices (CGMP) have not technically changed, interpretation by regulators is in a constant state of flux. CGMP regulations are very broadly stated guidelines not constrained by detailed regulatory requirements. With guidelines it is possible to functionally incorporate technological advances, procedural changes or industrial advancement of what was previously called "best practices." This explains why the very name of the regulation was changed by the FDA to Current Good Manufacturing Practices to add emphasis to the fact these are dynamic standards.

This is based on the very process of how the FDA inspects vaccine manufacturers. Several years ago, the FDA established Team Biologics and increased the emphasis on CGMP quality issues for all biologics companies, starting with blood products manufacturers and moving to vaccine manufacturers.

The requirement that vaccine manufacturers stay current with technological advances has necessitated a significant and ongoing investment in facilities, including older facilities in which older commodity priced products are produced. These requirements are sometimes put into effect even in the absence of any demonstrated concerns with the vaccines produced in those facilities. New investments have also been made necessary in process validation, and in the hiring and training of personnel with high levels of expertise needed to ensure that long-term CGMP quality standards are being met and sustained. The important point for a discussion in strengthening supply is that we must be realistic about the necessary investments in time and money involved in operating a modern vaccine production facility, even while manufacturing products that were licensed decades ago and continue to be produced safely and effectively.

Return on Investment

As I mentioned earlier, a major cause of supply fragility is what has been characterized as a poor potential return on investment, particularly for older vaccines. Historically, vaccine purchasers have wanted to treat vaccines as commodities, even though they are not, and the system has driven prices down. Raising prices can be difficult, or impossible, yet ongoing investments are

required to meet evolving CGMPs and to develop improved formulations. It should be no surprise that, when manufacturers find themselves holding low margin commodity products with increasing production costs, some choose to opt out. In order to ensure that we have state-of-the-art formulations and the most modern way to produce them, manufacturers should be encouraged to invest in infrastructure rather than disincented as is too often the case today.

What We Don't Need

Industry is up to the challenge of producing childhood vaccines which are safe, effective and in sufficient number of doses to immunize America's children.

Several proposals in Congress would undermine incentives for existing and potential manufacturers to produce vaccines. Whether called "national vaccine authority" or "GOCOs" (Government-Owned, Company Operated), the common theme of these proposals is to have the federal government get into the business of manufacturing vaccines.

Government competition would stifle new vaccine entrants into the market without guaranteeing any more supply of vaccines and requires the limited universe of top scientists in the field to develop them.

There are no shortcuts to making vaccines. It is a long, expensive and cumbersome process – a process which the government would have to go through before its first dose ever reached the market – probably at least a decade from now. A GOCO would not have alleviated any of the recent shortages experienced in the U.S.

A GOCO would not result in faster changeover of production lines than commercial plants in the event of a vaccine shortage, and wouldn't be able to switch from one vaccine to another. Usually you can't even use the same lines for spore, fermented, viral products and particularly bioterrorism agents. Even if it were possible it requires special air handling, multiple re-inspections before switchovers to prevent contamination. Different vaccines require different features on filling lines. These features need to be re-standardized and tested every time a change occurs. No plant could simply have switched to produce influenza or DTaP. Different complements of technicians may well have to work on different lines given exposure risk issues. If one vaccine exposure problem occurred it would cause a ripple of inspections to all lines to prevent cross contamination. Even government vaccines would need to be safe and effective.

It is often overlooked that it is science, not manufacturing, that is the limiting factor in developing new vaccines. All the manufacturing capacity in the world can't produce a vaccine until science develops the product.

What We Do Need – Strengthening Vaccine Supply

Today we offer six proposals to ensure a stronger vaccine supply. They involve cooperation, between government and industry providers and, we believe, will have a positive impact on strengthening our system by building on what is already in place.

1) We support expanded stockpiles for use if supplies are disrupted

We support additional funding for the CDC to establish stockpiles for both single and multi-source products. In recent years, the number of vaccine stockpiles has decreased. It is time to look at how to use them as a significant source of stabilization of supply in the face of unforeseen fluctuations or the loss of a manufacturer for which advance notice cannot be provided.

For example, had there been a national tetanus stockpile we would not have had the shortages we recently experienced while the remaining company expanded its production – a process that takes up to a year.

It has been suggested that such a stockpile would cost some $750 million but we believe that is a worthwhile expenditure for the nation's health. The recently-passed bioterrorism bill includes authorization for stockpiles for bioterrorism vaccines but not childhood vaccines.

2) Use the expertise of vaccine manufacturers to help formulate sound immunization policy.

Manufacturers have and continue to have ongoing information discussions with policymakers and government officials at agencies like the CDC. This is because manufacturers can provide realistic assessments and expertise about how vaccines are developed and produced, the challenges in doing so as well as a view into how providers practice and use vaccines. We deal with tens of thousands of providers each year, public and private, and cutting across the specialties, and we can share our insights to help improve delivery. It is important that those making vaccine policy, both on staff and on expert committees, have this expertise available to them. However, in more formalized settings, this is no longer occurring. An example is CDC Working Groups where industry representatives are no longer permitted to fully participate in discussions. To exclude industry from these considerations risks that regulations and guidance will be based on incomplete information that could result in wasted resources, inefficient implementation of policy changes and ultimately a loss of faith in our immunization system. We are a resource that should be

used. Making policy in a vacuum is a recipe for future supply problems.

Industry does not expect to participate in decision-making but, given the limited universe of vaccine expertise, government can benefit from the views of vaccine experts in industry.

3) Government and advisory bodies need to act with greater predictability

Continued uninterrupted manufacturing and distribution of vaccines is dependent upon reasonably predictable action by government agencies and advisory committees as well as open lines of communication between those bodies and the manufacturers. Government agencies and advisory committees need to be aware that changes in manufacturing or other regulatory policies could impact future supply, and should take such possibilities into consideration when proposing new policies. Specifically, we suggest that government agencies and advisory committees need to allow adequate advance notice whenever manufacturing changes are necessary. Simply put, if the changes are required before manufacturers can make them and the FDA can approve them, shortages will occur. To this end, the regulatory and guideline process needs to be kept predictable, without abrupt changes in requirements of guidelines and with ample opportunity to communicate about the implications.

4) The Vaccine Injury Compensation Program should be strengthened.

The Vaccine Injury Compensation Program stabilized our national immunization program since the late 1980's, reducing the frequency of the liability uncertainty that had destabilized the industry. The VICP provides a system of compensation and requires that injury claims be litigated initially within the VICP. Prior to its enactment, litigation had left a trail of national shortages and instability of supply of essential childhood vaccines. Recently, new strategies have emerged for vaccine injury claims which are intended to circumvent the Program. Once again, manufacturers are facing liability exposure that measures in the billions of dollars. This trend is evidenced in large part by the upswing in the number of lawsuits primarily involving Thimerosal. We are concerned that, without a re-doubling of the effort needed to address these issues, we will once again be in the same position that we were in nearly twenty years ago, this time encompassing both pediatric and adult vaccines. We propose strengthening the existing VICP effort.

Recently, Senator Frist introduced a thoughtful and comprehensive vaccine bill, S. 2053. It contains a section on VICP, which adopts the recommendations of the Advisory Commission on Childhood Vaccines to make the system more user friendly.

In addition, it reiterates that the intent of VICP is that vaccine claims proceed initially through the program. We strongly recommend the provisions of the Frist bill to you.

5) Strengthen our messages that prevention is the most desirable intervention.

A reorientation of healthcare priorities to emphasize prevention over cure will provide incentives to doctors to immunize patients and to manufacturers to maintain their commitment to vaccine production.

Our society has traditionally preferred to pay for treating a disease rather than preventing it. People are prepared to spend thousands of dollars a year on a treatment once they contract a disease but will balk at paying modest sums to prevent it from ever happening. If we are to realize the potential of vaccines, we need to change that thinking. Otherwise, people will continue to gamble that they won't get a disease and use insurance if they lose.

There needs to be sufficient willingness to pay for preventive services. Recent reductions in CMS reimbursement are disincentives to physicians. Reimbursement rates should reflect the full value of vaccines including a realistic administration fee.

6) Heed the warning signs of a real and present danger – increasing lack of confidence in immunization.

The good news is that parents no longer fear many infectious diseases, because of the success of our immunization programs. Yet, they have also lost an understanding of the importance of vaccines, as they lack first hand experience or knowledge of the devastating damage vaccine preventable diseases can cause. It would be a failure of immense magnitude if we allow old and conquered scourges to regain a foothold because of misinformation. We urge you to look at ways to bring the public into the process and boost its confidence in immunization. There is as much of an urgent need to address misinformation about immunization as any other aspect of this issue. In a sense, the entire immunization enterprise is under siege

The vaccine enterprise in this country is a remarkable success story. I hope you will give consideration to the proposals we have laid out to protect and strengthen it. Fortunately, we have an industry that wants to partner with government and with all elements of our nation's immunization enterprise to achieve even greater successes.

Thank you very much for your attention and your commitment to the immunization system in this country.

Testimony
Before the Committee on Governmental Affairs
United States Senate

Protecting our Kids: What is causing the current shortage in childhood vaccines?

Statement of
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Director, National Immunization Program
Centers for Disease Control and Prevention,
U.S. Department of Health and Human Services

For Release on Delivery
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Introduction

Good morning Mr. Chairman and members of the Committee.

I am Dr. Walter Orenstein, Director of the National Immunization Program at the Centers for Disease Control and Prevention (CDC). The Committee requested that CDC testify about the current childhood vaccine shortage. There are currently supply problems with five vaccines that provide protection against eight of the eleven vaccine preventable childhood diseases: Diphtheria, Tetanus, Pertussis (DTaP and Td vaccine), Pneumococcal infection (PCV-7 vaccine), Measles, Mumps, Rubella (MMR vaccine), and Varicella. Three of the four major manufacturers of childhood vaccines have recently had trouble producing adequate supplies of at least one of their products.

The current childhood vaccine shortages are unique and unprecedented. Several unusual and unanticipated factors have converged to create this situation. Health care providers and parents have been justifiably frustrated and worried by the shortages. The Department of Health and Human Services takes these concerns very seriously, and CDC is monitoring the situation in a variety of ways.

CDC was asked specifically to discuss the causes and extent of the shortages, their expected duration and impact, and CDC's role in maintaining the supply of childhood vaccines. We appreciate the opportunity to update you today on the current vaccine shortages and the steps CDC is taking to address the situation. Before I address these issues, I would like to point out

some good news - current information from manufacturers indicates that many of these shortages will be over before the end of the summer, and most will be resolved by the end of this year.

Background

Immunization is considered one of ten great public health achievements of the 20th Century. Indeed, vaccine preventable disease levels are currently at or near all-time lows, and childhood immunization coverage levels have been at all-time high levels during the last several years. This success is in no small part due to the innovative and highly effective role of the private sector (often in partnership with innovators in academia and government) in vaccine development and production in the United States and abroad, and the widespread use of licensed vaccines. Many of the childhood vaccines routinely recommended in the U.S. and elsewhere in the world, such as Polio, Measles, Mumps, and Rubella (MMR), *Haemophilus influenzae* type b (Hib), Hepatitis B, and Pneumococcal conjugate vaccines, were first brought to the market by private companies. Furthermore, competition among private pharmaceutical companies has resulted in substantial innovation, such as new and safer vaccines, which saves lives and prevents disease and disability.

For more than 15 years, our nation's children have had steady access to vaccines. The minor disruptions in production that have occasionally occurred in the past have been resolved through mobilizing vaccine from national stockpiles, and through the Food and Drug Administration (FDA), CDC, and partners working with manufacturers to increase vaccine supplies.

The Causes and Extent of the Current Vaccine Shortages

Causes: The causes of the current childhood vaccine shortage are multi-factorial and complex. We cannot point to any single reason for the shortage, but rather must look at specific issues affecting shortages of specific vaccines. There is no apparent single characteristic of any of these vaccines at the root of the shortage. Vaccines included in the shortage are both new, such as Pneumococcal Conjugate vaccine (PCV-7), and long-standing, such as Measles, Mumps and Rubella vaccine (MMR).

In general, marketplace and economic factors play an important role in vaccine supply. The fact that there are relatively few manufacturers producing vaccine means that any disruption in one manufacturer's production has a major impact on the vaccine supply. This problem is particularly acute when there is only one manufacturer for a vaccine, which is the case for three of the vaccines that have been in short supply. Vaccines, in general, may not compete well financially with other pharmaceutical products within a company, which may lead to business decisions to decrease or stop vaccine production. Economic issues are clearly critical to the long-term viability of the vaccine industry. However, such issues may not have been the immediate cause of many of our current problems.

We do not have access to data on production and development costs or profits, but we do have access to price data for the public sector and catalog prices for the private sector. Shortages are occurring with vaccines that range widely in cost (Figure 1), an indication that low prices for

some of the vaccines may not be the main factor in the shortages. Four of the five vaccines for which there are supply problems (PCV-7, Varicella, MMR, and DTaP) had relatively high prices, ranging from $11.75 per dose to $45.99 per dose on the Federal contract. In contrast, the three vaccines without supply problems range in price from $7.63 to $9.43 per dose. If economics were the single most critical driving factor in this situation, we would have expected to see shortages of the lower priced, and presumably less profitable, vaccines.

Some of the factors that are contributing to the current shortage include manufacturers' production capacity, regulatory compliance issues, manufacturers' business decisions to stop producing certain vaccines, and decreases in production yields caused by changing to single-dose vials to remove the preservative thimerosal from one of the vaccines.

In some cases, manufacturers of vaccines currently in shortage recently implemented changes in their production practices that contributed to decreased vaccine output, usually of a temporary nature. Some of these changes were related to manufacturing problems and others related to efforts to comply with current Good Manufacturing Practices (cGMP). FDA is addressing the cGMP issues in their testimony in more detail.

Unanticipated and abrupt business decisions by some manufacturers to leave the market have also had an impact on the vaccine supply, particularly in the case of vaccines containing tetanus and diphtheria toxoids (Td and DTaP). For example, when one major producer stopped making Td, the remaining company was unprepared to immediately fulfill the resulting supply needs. In

the case of DTaP vaccine, two of the four manufacturers abruptly discontinued production. Further, one of the two remaining manufacturers made changes in production as part of an effort to remove thimerosal, a mercury-containing preservative, from its DTaP vaccine. While there is presently no scientific evidence showing any causal association between thimerosal and adverse events, these changes were made in response to Public Health Service (PHS), American Academy of Pediatrics (AAP) and American Academy of Family Physicians (AAFP) precautionary recommendations, intended to reduce overall exposures of infants to mercury in a setting where other exposures to mercury (e.g. food, environmental) were more difficult to control. The removal of thimerosal as a preservative for these pediatric vaccines was accomplished through switching from multi-dose to single dose packaging. Packaging vaccine in single dose vials requires a greater volume of vaccine per dose compared to multi-dose vials, to ensure that a full dose can be drawn from the vial, resulting in fewer doses available for distribution.

Extent: While the shortage is considered national in scope, the extent varies by vaccine, with some shortages being more widespread than others. Vaccine manufacturers with whom CDC has contracts routinely submit quarterly Biologic Surveillance Reports to CDC showing total numbers of doses of vaccine distributed nationally, through both public and private purchase. When pre-shortage and current distribution data are compared, the vaccines most significantly affected appear to be Td and Pneumococcal vaccine, which both show a 40% decrease in doses distributed nationally. There was a less dramatic decrease in doses of varicella vaccine distributed; between 26% and 29%, depending on the periods compared. The MMR shortage was

alleviated in part by drawing from an existing CDC stockpile, but there still has been a 15% reduction in doses distributed.

Shortages have also varied by location and health care provider. Some health departments, clinics, and physicians have adequate supplies of vaccines, while others are experiencing vaccine shortages or delays in vaccine delivery.

The Duration and Impact of the Current Vaccine Shortages

Duration: Some vaccines have been in short supply longer than others. Shortages of each vaccine did not start at the same time, and supply has varied month to month. How long the shortage is expected to continue also varies by vaccine, but several shortages are likely to be improving or resolved in the next 2 to 4 months. Predicting the duration of the shortages is dependent on manufacturer projections. These projections are continuously adjusted as the situation evolves.

In general, manufacturer projections indicate that the situation is rapidly improving. Based on information just received from the manufacturer, we anticipate returning to the routine schedule for Td around the end of this month. CDC will shortly make an announcement about this. The FDA licensure on May 14, 2002 of a new DTaP vaccine brought additional DTaP vaccine to the market. Since approval on May 14th, FDA has released five lots of the vaccine, which could alleviate the DTaP shortage more rapidly. Based on information just received from one of the the

manufacturers, we anticipate that the DTaP shortage will be resolved soon. Also, according to the manufacturer, the supply of MMR and Varicella vaccines should be improving in June, and the shortage is expected to be resolved by the end of July and August, respectively. Our most significant and enduring problem appears to be with pneumococcal conjugate vaccine; according to manufacturer projections, pneumococcal conjugate vaccine will be in short supply through this fall and probably into 2003.

Impact: The impact of the shortage is being felt by health care providers, schools, and parents. The Advisory Committee on Immunization Practices (ACIP), with concurrence from the AAFP and the Committee on Infectious Diseases of the AAP, has made several temporary changes in routine immunization recommendations. These changes prioritize limited vaccine supplies to the most critical doses in the schedule for the most vulnerable children. However, this means that health care providers are sending children home without giving them all of their normally recommended vaccines. For example, the ACIP recommended that providers having supply problems with DTaP should defer vaccination of children aged 15--18 months with the fourth DTaP dose. If deferring the fourth dose does not leave enough DTaP to vaccinate infants, then the fifth DTaP dose (given to children aged 4--6 years) also should be deferred. Giving fewer than the usually recommended number of doses of PCV-7 vaccine to infants is another example of the revised recommendations. Sometimes, even when providers have been following the revised recommendations, they have still run out of vaccine. This puts children at risk, and puts a significant burden on providers to keep track of children they weren't able to immunize and recall them later.

School immunization requirements have also been affected, because supplies have not been adequate to assure that children in need of immunizations can get them. School requirements have been one of our most effective interventions to prevent outbreaks of vaccine-preventable diseases among school-aged children. School entry requirements for vaccines in shortage have been temporarily suspended in some states. A recent survey of state immunization programs found that 48% of states have made changes to their school entry requirements for Td, and about 10% have made changes to their school and daycare requirements for DTaP. When vaccine supply improves and the rules are reinstated, school staff will have to ensure that children missing required vaccines have received them. Finally, parents have experienced frustration and anxiety when they have made the effort to bring their child in for vaccinations, and have been told the child could not receive all the recommended vaccines during that visit.

While it is impossible to predict the larger public health impact of the current childhood vaccine shortages, there is clearly an increase in vulnerability to disease when children remain unvaccinated. CDC is carefully monitoring disease surveillance and immunization coverage data to assess the ongoing impact of the shortage. So far, there is no evidence of outbreaks related to the shortage.

CDC's Role in Maintaining the Supply of Childhood Vaccines

Vaccine Ordering and Distribution: CDC has contracts with all childhood vaccine

manufacturers, through which states and other grantees purchase vaccine with public funds, including Vaccines for Children (VFC), Section 317 of the PHS Act, and state funds. A comparison of public childhood vaccine purchases with Biologic Surveillance Reports data on the total childhood vaccines distributed in the U.S. for calendar year 2000 shows that CDC's contracts accounted for 52% of the national childhood vaccine supply. To encourage multiple manufacturers to enter the market, contracts are sought for all licensed vaccines, with quantities purchased for each dependent on state and individual provider choice. CDC is monitoring state vaccine orders, in an effort to see that the vaccines in shortage purchased through our contracts are distributed equitably. For example, CDC has restricted the number of doses states may order, based on the amount of vaccine they have in stock, and on the population in their state eligible for public vaccine.

ACIP Recommendations: CDC is working closely with the AAP, the AAFP, and the ACIP, which has recommended changes to the immunization schedule for each affected vaccine. These recommendations prioritize using available supply for the most vulnerable children, and include deferring booster doses and doses given later in the series. CDC has been working closely with state immunization programs and health care provider organizations to inform concerned parties about the recommended changes. Revisions to the schedule are described in detail on CDC's website (www.cdc.gov/nip).

Vaccine Stockpile: What is frequently referred to as the national vaccine stockpile is not, in actuality, a static, stand-alone warehouse of vaccine stored for emergency use. In order to ensure potency and safety, vaccine stockpiles must be continuously rotated and replenished. Therefore, CDC's approach has been to establish Storage and Rotation Contracts with manufacturers, frequently referred to as stockpiles. These contracts are essentially a mechanism for CDC to purchase vaccine over and above the national need from manufacturers, so that there is vaccine available to draw from in the event of an interruption in production.

The first "Storage and Rotation Contract" was initiated in 1983, when funding for the CDC stockpile was provided through Congressional appropriations to establish a 6-month strategic supply of each vaccine universally recommended at the time, including DTP, OPV, and MMR. Since 1983, stockpiles of vaccine have fluctuated according to funding appropriations, the immunization schedule, and whether there is a Federal contract for the vaccine. Two statutory authorities support CDC establishing and maintaining a six-month vaccine supply in stockpiles. They appear in the Vaccines for Children (VFC) Program statute and as a note to the National Childhood Vaccine Injury Act of 1986, as amended (NCVIA). Section 317 of the PHS Act (42 U.S.C. 247b) also provides authority to stockpile vaccines. Using VFC funds, CDC currently maintains stockpiles of three pediatric vaccines: MMR, e-IPV, and DT.

Stockpiles have been very effective in the past in alleviating brief disruptions in vaccine supply, and are an important resource to maintain. Between 1984 and 2002, CDC stockpiles were drawn on multiple times, when supplies of four different vaccines (OPV, DTP, E-IPV, and MMR) were

interrupted. The interruptions were due to a variety of factors, and affected several manufacturers. Events precipitating the need to draw from the stockpile in the past have included fire damage at a vaccine production plant, production problems, such as disruptions in filling and packaging lines, and quality assurance difficulties. When such interruptions in production occurred, CDC and the manufacturers were able to fall back on supplies of vaccine established through the Storage and Rotation Contracts, or stockpiles, to fill a temporary need. Usually, rather than distributing vaccine directly from the stockpile, CDC allows the manufacturer to borrow from it. Typically, vaccine taken out of the stockpile is replaced within a year.

Managing stockpiles effectively presents unique challenges. First, there is the issue of storage and maintaining continuous rotation of the stock. Maintaining excess inventory so that vaccine will be available for emergency use may be costly, not only in terms of vaccine, but also in terms of the facilities required for storage. Next, as new vaccines are developed, some old ones become obsolete; for example, oral polio vaccine has been replaced with inactivated polio vaccine, and whole cell DTP vaccine with the acellular pertussis DTaP vaccine. In order to minimize the financial risk of stockpiling vaccines that may not have a reliable future, the CDC approach in purchasing vaccines intended for a stockpile has been to prioritize vaccines that are routinely recommended, fully implemented, and have a single manufacturer. For example, MMR has consistently been included in the immunization schedule since its development, and has been stockpiled since 1983. Vaccines with multiple manufacturers, such as DTaP, Hepatitis B, and Hib vaccines, represent further complications in stockpile management. In such cases, the market share for each brand of the vaccine must be carefully evaluated to determine how much of

each product should be stockpiled by each manufacturer. Storage and Rotation Contracts may need to be renegotiated if market share changes significantly among the companies. Finally, new vaccines pose unique challenges for stockpiling, as their demand is unclear and time is required to produce enough doses to be able to set aside an emergency supply.

Maintaining Communication with Manufacturers, the Public, and Health Care Providers: The CDC is in constant communication with vaccine manufacturers regarding the status of vaccine production. CDC provides weekly vaccine supply updates on its website. This information is intended to help states and health care providers plan their immunization strategies, based on available vaccine supply. The website also provides links to state health departments, so parents and the public can find out more about local vaccine availability.

Options Under Consideration for Alleviating Current and Preventing Future Shortages

In addition to consulting with other HHS agencies, such as FDA and Centers for Medicare & Medicaid Services (CMS), CDC is working with its partners in industry and with other groups to better understand the current shortages, identify potential short-term solutions, and prevent future shortages. What we learn from the current shortages should help us prevent or mitigate future shortages. Since the causes are multiple and complex, no single solution is likely to prevent future shortages. The partners we are working with include the ACIP, the AAP, the AAFP, the Association of State and Territorial Health Officials (ASTHO), state immunization programs and vaccine manufacturers.

In addition to the input CDC is gathering from its partners, the National Vaccine Advisory Committee (NVAC) and the U.S. General Accounting Office (GAO) are conducting independent reviews of the situation. This past February, NVAC held a meeting with many of the stakeholders in vaccine supply including representatives of federal and state governments, vaccine manufacturers, and private providers. A report with recommendations for preventing future shortages is expected from NVAC later this summer, and HHS is looking forward to reviewing it.

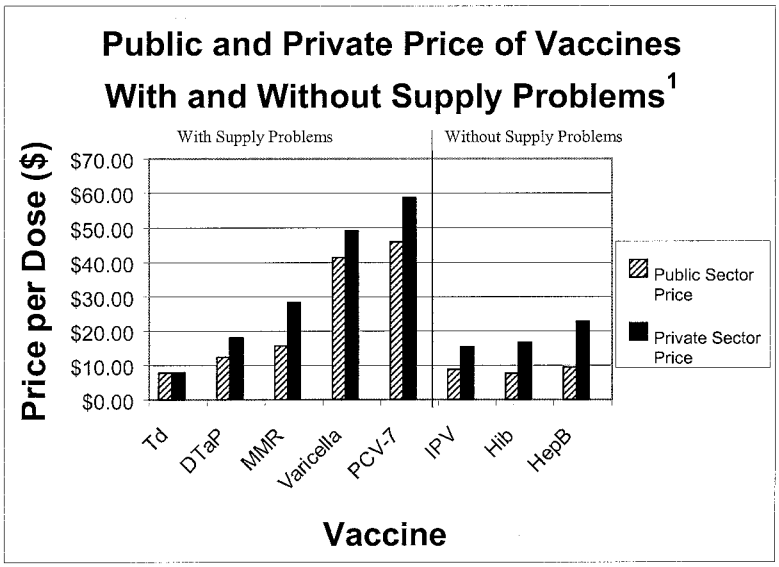
Early this year, GAO began working on a review requested by several legislators, designed to address factors relating to the current vaccine shortages. GAO is expected to release their report in late July.

Conclusion

The current childhood vaccine shortages are complex, unprecedented in scope and result from a number of factors. CDC has implemented a number of short-term measures to facilitate the efficient and effective use of available vaccine. CDC is also receiving input from a number of organizations regarding strategies to prevent such shortages in the future, and we look forward to hearing their recommendations.

Thank you for the opportunity to tell you about the current childhood vaccine shortages. At this time, I would be happy to answer your questions.

Figure 1



[1] Federal contract and private sector prices as of May 20, 2002
[2] There is not a Federal contract for Td; on May 28, 2002 the market price ranged from $7.78 (MN Multistate contract) to $7.91 (manufacturer catalog) per dose.
[3] DTaP, Hib, and Hep B prices are averages of multiple manufacturers' prices

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT

OF

LESTER M. CRAWFORD, D.V.M., Ph.D.

DEPUTY COMMISSIONER

FOOD AND DRUG ADMINISTRATION

BEFORE THE

COMMITTEE ON GOVERNMENTAL AFFAIRS

UNITED STATES SENATE

JUNE 12, 2002

RELEASE ONLY UPON DELIVERY

Introduction

Mr. Chairman and Members of the Committee, I am Dr. Lester Crawford, Deputy Commissioner, Food and Drug Administration (FDA or the Agency). I appreciate the Committee's interest in the current shortage of childhood vaccines and welcome the opportunity to participate in this hearing. FDA is concerned about the fragility of the Nation's vaccine supply and is committed to the availability of safe and effective vaccines to protect our children and ourselves from many serious infectious diseases.

Recently there has been an unanticipated shortage of some of the recommended vaccines in the United States. The pediatric vaccines that have been or are in short supply include Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP); Measles, Mumps and Rubella Vaccine (MMR); Varicella (chickenpox) Vaccine; and Pneumococcal-conjugate vaccine. Tetanus and Diphtheria toxoids adsorbed for adults (Td) has also been in short supply, and delays in the availability of influenza vaccine have occurred in the past.

I am happy to report that several of these shortages are easing. FDA's recent licensure of a new DTaP vaccine manufactured by Aventis Pasteur, Limited, and their recent announcement of an increased supply of Tetanus and Diphtheria Toxoids, means that relief in the shortage of these two products is in sight. The manufacturer has reported to its customers that the MMR vaccine shortage has eased and that the Varicella vaccine shortage will likely improve soon. In the case of Varicella, the supply will be sufficient to return to the recommended schedule by August or September, although additional time will be needed to build up inventory. Due to manufacturing challenges as well as an unexpected demand for Pneumococcal-conjugate vaccine, this vaccine is still in short supply for the foreseeable future. An ample supply of

Influenza vaccine is expected for the 2002-2003 influenza season, and no delays are anticipated at this time.

Potential Causes of Vaccine Shortages

Vaccine shortages can stem from a number of causes and the more recent shortages are not due to any single factor. In fact, the recent shortages stem from a number of factors including: 1) the withdrawal from the market of one manufacturer, 2) difficulties in manufacturing processes, 3) temporary shutdowns of facilities for upgrades or maintenance, or to correct manufacturing deficiencies observed by the manufacturer or FDA during inspections, and 4) other factors, such as transition to thimerosal-free vaccine formulations.

Given the complexity of biological materials and manufacturing, and the need to maintain quality and consistency during production, manufacturers may experience problems achieving the desired production yields or maintaining quality of final materials. As a result, production delays or shortages often surface. Vaccine manufacturers may decide to change or improve their processes, to renovate and update their facilities or to perform regular maintenance. When this process takes longer than expected it can result in decreased vaccine production. Occasionally, manufacturers will issue voluntary recalls that have an impact on vaccine supply. Although the manufacture of biologic products is complex and demanding, and the need to update and maintain modern facilities is costly, the current prices paid for many vaccines are comparatively low compared to the prices of many other drug products. Manufacturers may choose to discontinue production of a vaccine (or of vaccines altogether) as a business decision, such as when they believe that the production and sale of a particular

vaccine or needed investments in manufacturing facilities are no longer economical. When there are a limited number of manufacturers for a particular vaccine, the impact of one firm withdrawing from the market may cause a significant shortage. If other manufacturers are available and willing, considerable time may be needed to increase production to respond to a shortage. Many vaccines require a year or more of production time.

A temporary shortage may occur when the public health community alters existing vaccination recommendations. For example, the Advisory Committee on Immunization Practices recommended that influenza vaccine be administered to a wider-age range of people in 2000-2001. If implemented, this recommendation would have meant that in order to meet demand, manufacturers would have to increase production. However, production limitations prevented the implementation of the new recommendation.

Similarly, the response by manufacturers to the recommendation by public health officials that the mercury-containing preservative (thimerosal) be removed from routinely recommended pediatric vaccines in an effort to reduce mercury exposure in children exacerbated the shortage of DTaP vaccines that arose when one of the three major manufacturers of DTaP decided to withdraw from the market in 2001. One approach to eliminate the need for a vaccine preservative is to change from a multi-dose to a single-dose presentation. However, manufacturing for a single-dose presentation means that the filling-line capacity must be increased. According to one manufacturer, more vaccine is lost through overfilling of single-dose vials than multi-dose vials. This significantly reduces the number of doses of vaccine available from each production lot or batch.

A shortage may also stem from a firm deciding to temporarily suspend operations to improve manufacturing practices, or to correct deficiencies identified during an internal review of its operations or by an FDA inspection. Firms often initiate corrective action independent of FDA regulatory action, in order to ensure production quality. When FDA inspects a vaccine manufacturer and finds deficiencies, the Agency carefully considers the impact on product availability before taking action. In some situations, the Agency may determine, after balancing all factors, that a decrease in the availability of a "medically necessary product" could pose a substantial risk to patients. In such cases, FDA regulatory action may allow manufacturing of the critical product to continue, provided that certain conditions are established to ensure product safety. The Agency evaluates each circumstance on its own facts, balancing the medical need for the product against the safety assurances in place before product is released for use.

While FDA works proactively and interactively with manufacturers to address shortage issues, it is important to note that FDA does not have the authority to require manufacturers to stay in the market and produce a given vaccine, nor does FDA have the authority to direct manufacturers to increase production when a shortage occurs.

FDA's Response to Vaccine Shortages

FDA is constantly working with National of Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and with industry to take whatever steps possible to prevent and alleviate vaccine shortages. We work to maintain open and continued dialogue with vaccine manufacturers, and assist firms who may seek licensure and to enter the vaccine

manufacturing market. FDA routinely meets with manufacturers prior to submission of a licensing application to facilitate the regulatory process and provide guidance on requirements for new vaccines. The Agency also encourages and works with manufacturers to enhance their production capabilities and capacities through meetings, teleconferences, review of submissions and related regulatory activities.

Whenever possible, FDA informs manufacturers of potential shortages to allow them to reallocate product to those who need it most and to take action to increase product inventory. In addition, FDA works with manufacturers that want to correct manufacturing deficiencies in order to avoid shortages of critical products. In October 2000, for example, one of the manufacturers of influenza vaccine entered into a judicially approved consent decree of injunction. Under the decree, the manufacturer was able to continue distributing influenza vaccine, and FDA worked with the manufacturer to develop a satisfactory compliance plan to help ensure the safety and availability of this medically important product. As a result, this company, a major supplier of influenza vaccine in the United States, was able to supply vaccine for use during the 2000-2001 flu season. In contract, another manufacturer of influenza vaccine decided not to take action to correct manufacturing problems. Instead, it elected to withdraw from the market in 2000.

Several other manufacturers of influenza vaccine experienced decreased production yields due to the slow growth of one of the influenza strains used in the vaccines. This development led to a temporary delay in vaccine availability, which created temporary spot shortages. To address this situation, in early 2001, FDA contacted each of the three remaining influenza

vaccine manufacturers to discuss their projections for influenza vaccine production and facilitate any possible expansion of manufacturing capacity. Two manufacturers submitted supplements to their licenses for changes in their manufacturing process that allowed for increased capacity or production. These manufacturing changes led to an increase in the production of influenza vaccine for the 2001-2002 season, with a shorter delay. As a result, the greatest number of doses ever produced in a given year was released for the 2001-2002 season (approximately 87 million doses).

Licensing Process and Assuring Vaccine Safety

Vaccines are different from most drugs in several respects and achieving the highest quality in manufacturing is especially challenging and critical. First, they are most often produced from or use living cells and organisms, as well as complex growth materials derived from living sources. Thus, the potential for contamination is higher than for most drugs, so the quality and purity of all source materials must be carefully monitored. In fact, a separate Federal entity for regulating biological products was first established, well before the FDA itself, under the Biologics Control Act of 1902. Congress took this step following an incident in which horse serum intended for the treatment of diphtheria actually transmitted tetanus, killing 13 children. Second, the production of most preventative vaccines requires growing the immunizing agent, i.e., bacteria, viruses, etc. in the production facility, and the subsequent purification of complex molecules from these organisms. Growth conditions are complex, and subtle changes in materials, in the process itself, or in conditions such as temperature can result in changes in the final vaccine that can affect its safety, its effectiveness or both. Third, the final vaccine itself is usually not, like most drugs, a simple molecule that can be tested for

its purity and potency using simple chemical and physical methods. Instead, each lot of vaccines must be carefully tested for its composition and potency, through the lot release process. Finally, unlike most drugs, which are given to people to treat an illness, vaccines are administered to large numbers of healthy people to prevent infectious diseases. For this reason, even very rare adverse effects are generally not viewed as acceptable to healthy children and adults. For all of these reasons, the entire process of vaccine manufacturing is highly demanding and complex, and both the licensing of vaccines and the regulation of vaccine production is subject to the highest expectations and standards.

FDA's regulatory responsibilities with regard to vaccines can be divided into pre-approval and post-approval activities. Prior to licensure of a vaccine, sponsors (most often manufacturers) conduct clinical trials to generate safety and efficacy data that can be used as a basis for approving a marketing application. For studies conducted under an Investigational New Drug Application (IND), FDA provides guidance on clinical trial conduct and design. Foreign clinical studies not conducted under an IND also can be used in support of a marketing application if they were well designed, well conducted, performed by qualified investigators, and properly conducted to protect the rights and safety of the study participants.

Under the regulations, vaccines not licensed for use in the U.S. may be used in the U.S. only as an investigational product under an IND application. The development of product under IND is usually sequential, beginning with safety testing in a small number of subjects (Phase I), following by dose-ranging and safety studies (Phase II), and a large trial for efficacy and safety (Phase III). Volunteers receiving an investigational vaccine must be fully informed

that the product is experimental and must give signed informed consent before they may receive the product. In order to obtain a license, a manufacturer has to submit a biologics license application. In many instances, trials are performed in foreign countries because the disease that the vaccine is intended to prevent has a higher incidence than in the U.S. and because the use of vaccines is increasingly global. For example, vaccines to prevention typhoid fever, Japanese encephalitis, pertussis, and hepatitis A have been licensed using efficacy data from clinical trials conducted in a foreign country. FDA applies the same standards to vaccine studies and manufacturing, wherever they are performed.

To obtain a license for a biological product, section 351(a) of the Public Health Service (PHS) Act requires a manufacturer to demonstrate that the biological product is "safe, pure, and potent," and that the "facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent." As part of these requirements, manufacturers must meet the standards established in FDA regulations applicable to biologics, including current good manufacturing practices (CGMP). CGMPs are established by the current industry practices and in FDA regulations (Title 21, Code of Federal Regulations (CFR) Parts 210 and 211). The term CGMP has its origin in the Federal Food, Drug, and Cosmetic (FDC) Act, section 501(a)(2)(B), which states that a drug is adulterated if "a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act as to safety and has the identity

and strength, and meets the quality and purity characteristics, which it purports or is represented to possess."

FDA determines conformity with CGMP and the standards set forth in the manufacturer's license primarily through inspection and surveillance, both before and after licensure. The goal is to ensure that consumers receive vaccines and other FDA-regulated products that meet the statutory requirements for safety and effectiveness. It is essential to recognize that CGMP non-compliance may affect the safety and effectiveness of a vaccine product, and therefore may place the public health at risk. Even seemingly minor CGMP violations, especially when they occur in multiples and are considered in aggregate, may indicate a systemic problem affecting product quality. The Agency strives for consistency in its inspections, paying particular attention to violations, such as contamination in the production facilities and processes, and looking for underlying systemic problems, such as lack of a documented and validated process, inadequate quality control, and repeated record-keeping omissions or errors.

Once FDA licenses a vaccine, we continue to monitor the product to help ensure continued safety and effectiveness. For vaccines, this is accomplished through ongoing review of adverse events reported through the Vaccine Adverse Event Reporting System (VAERS), post-licensure inspections, and other post-marketing activities. FDA performs inspections to determine whether manufacturers are following current good manufacturing practice and the standards set forth in their biologics license application. FDA may also perform targeted

inspections when, for example, there are changes to the manufacturing processes, facility, or equipment, or other significant events.

FDA also utilizes the mechanism of lot release review to help ensure quality and potency in the final vaccine that is distributed to consumers. Lot release plays an important role in FDA's vaccine regulations, by helping to assure the public that biological products are safe, pure, and potent. Because of the complex manufacturing process for most biological products, each lot of product undergoes thorough testing by the manufacturer prior to release for distribution. The manufacturer performs specific tests as set forth in its license application, such as those for sterility and potency. The manufacturer submits the results of its tests for potency, safety, and sterility to the Agency. The manufacturer also submits lot release protocols, and if applicable, product samples, before the product may be distributed in interstate commerce. The lot release program provides a quality control check on product specifications and is part of FDA's multi-part strategy designed to help assure biological product safety.

FDA's regulation of vaccine manufacturing is critical to maintaining public confidence in U.S. licensed vaccines. The importance of public confidence must be stressed. No other single health intervention has had the impact on disease prevention and our nation's health as immunization with U.S. licensed vaccines. For this reason, FDA carefully evaluates each licensing and regulatory action it takes, balancing the importance of product availability while working with manufacturers to help assure that products are as safe as current technologies allow will be distributed to consumers.

The Role of FDA Research in Promoting Vaccine Development and Availability

The complex and changing field of vaccinology presents both scientific challenges and opportunities for FDA. Maintaining FDA's core scientific expertise is critical to help assure quality review and quality products. First, FDA reviewers must maintain expertise to deal with changing basic, clinical and manufacturing sciences. Fostering an environment where such knowledge is current and valued helps to ensure that scientific reviewers, wherever possible, foresee or promptly identify important product issues with the potential to affect safety or effectiveness of a new or existing vaccine, perform a balanced assessment, and respond appropriately. Second, FDA research plays a unique and important role in improving the quality and availability of biologics, particularly in areas that affect multiple products and manufacturers. Every year FDA scientists help to provide to manufacturers new strains for the yearly influenza vaccine as well as biological standards for assessing the vaccine's potency. Ongoing FDA research on influenza is also designed to prepare for the possibility of another global influenza pandemic. These efforts by FDA reduce the need for duplicative efforts by manufacturers and shorten the time frames required for vaccine production every year. FDA scientists have also standardized assays for the potency of other vaccines, including those for acellular pertussis and polysaccharide-protein conjugate vaccines (e.g., Haemophilus type b conjugate and pneumococcal conjugate vaccines). FDA is conducting research to improve neurovirulence tests we hope may further enhance the safety of viral vaccines such as polio and mumps. FDA has also applied modern and novel technologies to the detection of potentially harmful contaminating agents in vaccines and the cell lines used to produce them, and these technologies are also applicable to new vaccines, such as for smallpox, urgently needed to help protect against the threat of bioterrorism.

A Collaborative Approach to Vaccines and Vaccine Policy Issues

FDA works proactively in collaboration with established interagency working groups and vaccine committees. Vaccine issues are a priority for the Agency and the Department of Health and Human Services (HHS or the Department). The Department has shown its commitment to vaccine issues through coordinating interagency groups to focus on vaccine safety and supply, among other issues. FDA participates as an ex officio member of the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP), the National Vaccine Program Office's (NVPO) National Vaccine Advisory Committee, and the Health Resources and Services Administration's (HRSA) Advisory Commission on Childhood Vaccines (ACCV). In turn, the CDC, NVPO, and NIH participate in FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC). These advisory committees have specific and unique responsibilities, and provide important opportunities for input from the public, including consumers, industry, and academia. FDA also participates in the Interagency Vaccine Group (IAVG) and its executive committee. The IAVG includes various HHS agencies and representatives from the U.S. Agency for International Development and the Department of Defense. FDA is also a member of an IAVG Working Group that is developing options to present to the Department to address the vaccine supply issues, and participated in a recently held vaccines shortage workshop held in February 2002.

Conclusion

Vaccines, licensed for use in the United States by FDA, have been protecting our nation's children from deadly infectious diseases for almost 100 years. In fact, immunizations

represent one of the most significant public health achievements of the 20th Century. Vaccines can be credited with saving more lives and preventing more illnesses than any medical treatment. Without question, continuing to ensure the availability of safe and effective vaccines is critical to protect the public health and to prevent disease outbreaks.

Mr. Chairman, I look forward to the recommendations of the ongoing study requested by the Congress concerning vaccine shortages and assure you that FDA will continue to be vigilant in searching out opportunities to enhance the supply of safe and effective vaccines.

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June 7, 2002

Honorable Senator Jean Carnahan
United States Senate
Washington, D.C.

Topic: Vaccine Shortages

My name is Robert Jay Hoffman, M.D., F.A.A.P. I am a practicing Pediatrician in the suburban St. Louis area. Our practice consists of ten providers in three locations seeing more than sixty thousand office visits per year. The vaccine shortage began approximately eighteen months ago and has had a direct impact on many of our families. This is true for many, if not all, of my colleagues and health departments in the St. Louis metropolitan area.

There has been NO routine adult dT (diphtheria/Tetanus) vaccine given to any of our high school children for more than fifteen months. The few doses left have been dedicated to those individuals suffering an injury, animal bite, etc., and must be administered in an emergency room. This is due to the fact that few, if any, private doctors have supplies remaining in their office. This necessitates higher out of pocket expense for emergency room visits. In addition, extensive record keeping is necessary to track each and every high school student who did not receive the recommended 15-year-old booster. I can assure your committee that it will be impossible to reach every student due to population mobility and other parameters outside the control of a private pediatrician, school nurse, or health department. We have been advised that supplies will trickle in during this summer with a price increase of greater than 200%!

In regards to a much newer vaccine called Prevnar, supplies have been so erratic that many of us never know if we will be able to vaccinate our infants from week to week. This vaccine is designed to protect infants and toddlers from the most common types of Pneumococcal blood infections and Meningitis. Without Prevnar infants are exposed to a greater risk of contracting this deadly bacteria. One has to wonder what liability is incurred, and by whom, should an infant contract this deadly disease. The shortages of Prevnar are ongoing to this very day.

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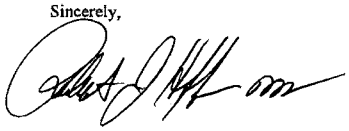
We have also experienced supply interruptions with Varivax, our chicken pox vaccine. In our practice alone, fourteen children have been hospitalized with severe complications of chicken pox in the last eighteen months. Also, if Varivax is not available to be administered simultaneously with the MMR (Measles, Mumps, Rubella) vaccine, then 30 days must pass to provide an optimal immune response. This necessitates another visit by the patient and another out of pocket copay forced on the family by several insurance companies. This delay and expense is caused purely by interruption in vaccine supply.

The most disturbing manipulation of vaccine distribution occurred in the St. Louis area during the past two Influenza seasons. Shipments were drastically delayed to private physicians and health departments for unknown reasons. Some of the parents of our high-risk children were able to receive Influenza vaccine at their place of employment prior to their chronically ill children receiving the vaccine. This put our high-risk patients such as asthmatics, diabetics, and heart patients at risk for Influenza due to delay in shipment. It caused our practice and many others in town to "ration" the few doses given to us by the manufacturers. We find this type of market manipulation intolerable and the manufactures should answer the obvious question as to why this occurred!

I have been asked by your staff members if we see the diseases meant to be eradicated by the routine childhood immunizations. The answer is a resounding YES! The most successful preventative measure in medicine is childhood immunizations. We must continue to provide these life saving immunizations on a timely basis according to the recommendations of the Centers for Disease Control and the American Academy of Pediatrics. The causes for supply interruptions must be discovered and corrected as soon as possible. Our children's well being is at stake.

I am truly honored to have been asked to submit this written testimony and wish for your committee's success in solving this important public health issue.

Sincerely,



Robert J. Hoffman, M.D.

Vaccine Shortage and Public Health Overview

By

Harold Bengsch, MSPH, REHS/RS

Director of Public Health and Welfare

Springfield/Greene County Health Department

Today as public health wrestles with issues of bioterrorism and other homeland security concerns, we are beset with a very real and important public health problem. For many years, public health's success in using vaccine to reduce morbidity and mortality of many diseases has been held up as the flagship for the success of preventive health practice. Today that very flagship is in danger of running aground.

Ever since the Institute of Medicine report, *"The Future of Public Health"*, was issued in 1988, state and local health departments have been working diligently to operationalize the "Core Function" of Public Health: **Assessment—Policy Development and Planning—Assurance**.

These functions are defined as:

- **Assessment** – The regular and systematic collection and analysis of community health statistics, health status, and needs.

- **Policy Development and Planning** – Utilizing a science-based process based upon "assessment" findings, a strategic approach will lead to the development of health policy that serves the public interest and need.

- **Assurance** – To achieve agreed upon goals established through policy development, which enlists public/private partnerships or by providing services directly whereby constituents are served.

With regard to immunization, the Core Function process has worked extremely well with childhood immunization rates nationally reaching levels never before attained. Today, these accomplishments are at risk. They are at risk primarily due to vaccine shortages and/or distribution problems.

No matter how well the *assessment* is done or how thoroughly *health policy* is thought out and developed, *assurance* of outcome is impossible when necessary resources are unavailable to fulfill the agreed upon policy(s).

In the case of immunizations, the critical resource is vaccine. The shortage of this necessary biological product was first seen in influenza vaccine approximately three years ago. Now, the vaccine issue has expanded into other antigens affecting childhood immunizations.

It is my concern, that when vaccine production rests solely with the private sector and in some cases with only one or two manufacturers who can withhold or cease production at will, risks of shortage for many reasons become predictable, but totally unpredictable as to when they may occur.

It is in this reality that public health finds itself today. Under these circumstances, excellent *assessments* and sound *policy development* become grounded on the reef of non*assurance*.

The purpose of this communication is to appeal to Congress to become a partner with public health in *assuring* an adequate supply of vaccine for our citizens. It is my belief that Congress is the **only** entity who can effect a workable solution to this problem.

If left unattended, the worsening disruptions in vaccine supplies can affect the immunization rates of our nation's children and adults. A decrease in herd immunity can be expected to lead to a resurgence of vaccine-preventable diseases. This would be an

inexcusable commentary on our nation's historical successful efforts in disease prevention.

If Congress will *assure* public health access to an adequate supply of vaccine, public health will meet its responsibility in *assuring* our communities receive this critical preventive public health intervention.

Please join with your partners in public health to *assure* this does not occur.

Thank you.

Vaccine Shortage Update
Cindi Kapica RN BSN
Immunization Coordinator
Springfield-Greene County Health Department
Springfield, Missouri
5/29/02

Serious shortages currently exist for several routine childhood vaccinations. Addressing the issues behind the shortages is paramount for continued public support of current immunization efforts. Vaccine manufacturers and public health officials can all agree that there is no one single reason for the occurrence of these shortages. The reasons are varied, as well as the proposed strategies for resolving these issues and preventing further shortages. Policymakers, physicians, pharmaceutical representatives, and public health officials must all work together to ensure that children are never denied vaccination opportunities due to a lack of available vaccine.

The following table was taken from the Centers for Disease Control website at www.cdc.gov/nip. This offers a brief a brief synopsis of the current issues facing many vaccine providers across the nation.

National Vaccine Supply Shortages			
Vaccine	**Shortage**	**Expected Duration**	**Temporary Change from Routine Recommendation**
Hepatitis B[1]	**No**		
Diphtheria, Tetanus, & Pertussis (DTaP)	Yes[2]	late summer 2002	**Yes http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5051a3.htm**
Td	Yes[3]	3rd or 4th quarter of 2002	**Yes http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5020a8.htm**
Haemophilus influenzae type B (Hib)	**See note[4]**		
Inactivated Polio (IPV)	**No**		
Measles, Mumps, & Rubella (MMR)	Yes	June/July 2002	**Yes http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5109a6.htm**
Varicella	Yes	June/July 2002	**Yes http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5109a6.htm**
Pneumococcal (PCV)	Yes	last quarter of 2002 or later	**Yes http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5050a4.htm**
Hepatitis A	**No**		

*Note: Only those vaccines included on the recommended childhood immunization schedule are included in this update.

Note[1]: There also is no shortage of Hepatitis B/Hib combination (COMVAX).

Note[2]: On May 14, 2002 the FDA gave licensure to Aventis Pasteur to distribute their second DTaP vaccine (DAPTACEL). This vaccine may be available by mid-June. There are now three DTaP vaccines (Tripedia, Infanrix, and DAPTACEL) distributed in the U.S.

Note[3]: Td supply is now available to providers other than hospitals. However, supply is not sufficient at this time to return to routine booster doses.

Note[4]: Hib vaccine is available from Aventis Pasteur. Hib vaccine orders from Wyeth require up to 60 days to fill and their supply is not likely to improve in 2002. Orders from Merck are taking 4 to 6 weeks to fill with little improvement expected before late 2002.

The following table is a compilation of the current issues locally as opposed to nationally. Consultation was conducted with the Missouri VFC (Vaccines For Children) office, and two large pediatric groups in Springfield.

Local Vaccine Supply Shortages for Springfield-Greene County Missouri Area			
Vaccine	Shortage	Children Being Deferred?	Utilizing Temporary Changes in Dosing Recommendations?
Hepatitis B	No		
Diphtheria, Tetanus, & Pertussis (DTaP)	Not locally	No	Not at this time
Td	Yes[1]	Yes	Yes http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5020a8.htm
Haemophilus influenzae type B (Hib) or Comvax (Hib/HepB combo)	Sporadic[2]	No	
Inactivated Polio (IPV)	No		
Measles, Mumps, & Rubella (MMR)	No	No	Not at this time
Varicella	Yes[3]	Yes	
Pneumococcal (PCV)	Yes[4]	Yes	Yes http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5050a4.htm
Hepatitis A	No	No	No

Note[1]: Is locally affecting both public and private sector vaccine providers

Note[2]: Private providers are currently experiencing shortages of Comvax. Hib single antigen vaccine is not commonly given due to the widespread use of the Comvax hib/hepatitis b combination vaccine. However, there are still instances when Hib as a single antigen is needed. Hib vaccine is available from Aventis Pasteur. Hib vaccine orders from Wyeth require up to 60 days to fill and their supply is not likely to improve in 2002. Orders from Merck are taking 4 to 6 weeks to fill with little improvement expected before late 2002.

Note[3]: Varicella (chickenpox) vaccine has been in short supply in the public and private sector at varying times in the past year. Currently, at the time of this report, the private sector in our area is extremely low and in some cases, supplies are exhausted. Our public health department has adequate supplies at this time.

Note[4]: At the time of this report, the private sector reports adequate supplies of this vaccine, however, our public health department has an extremely low stock.

Locally, specific details of the vaccine shortages are subject to change from week to week. According to the Centers for Disease Control, there are several different reasons for these shortages. These include companies leaving the vaccine market altogether, manufacturing or production problems, and insufficient stockpiles. Consequently, some shortages may be specific to one manufacturer.

The disruption of herd immunity is the greatest fear among public health experts. The assumption of the majority of parents and vaccine providers is that adequate vaccine supplies exist. We have enjoyed the benefits of higher immunization rates of our nation's children and adults, which have been evident in contributing to the

dramatic decrease in vaccine-preventable diseases. When this supply chain is disrupted, and routine doses for children are deferred indefinitely, it creates a population-based ripple effect.

Private and public vaccine providers alike, are concerned that the basic level of trust from parents and patients will diminish over time. It is the provider who must answer to the parent of a child who may not receive a dose of vaccine due to a manufacturing issue. Providers stress the importance of timely vaccinations to parents, but are not able to guarantee them from week to week whether that vaccine will even be available. Credibility is a prevailing issue that helps to ensure our nation's children and most vulnerable are vaccinated on time, every time. Without it, we may see overall immunization rates go in a downward trend.

Thank you for the time you are spending on this very important issue. I would be happy to provide you with any further information you might need.

Sincerely,

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