A REVIEW OF THIS YEAR'S FLU SEASON: DOES OUR PUBLIC HEALTH SYSTEM NEED A SHOT IN THE ARM?

HEARING

BEFORE THE

COMMITTEE ON GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

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A REVIEW OF THIS YEAR'S FLU SEASON: DOES OUR PUBLIC HEALTH SYSTEM NEED A SHOT IN THE ARM?

THURSDAY, FEBRUARY 12, 2004

HOUSE OF REPRESENTATIVES,
COMMITTEE ON GOVERNMENT REFORM,
Washington, DC.

The committee met, pursuant to notice, at 10:19 a.m., in room 2154, Rayburn House Office Building, Hon. Tom Davis (chairman of the committee) presiding.

Present: Representatives Tom Davis, Duncan, Miller, Waxman, Tierney, Van Hollen, and Norton.

Staff present: Melissa Wojciak, staff director; David Marin, deputy staff director/communications director; Ellen Brown, legislative director and senior policy counsel; Drew Crockett, deputy director of communications; Susie Schulte, professional staff member; Teresa Austin, chief clerk; Brien Beattie, deputy clerk; Phil Barnett, minority staff director; Anna Laitin, minority communications & policy assistant; Sarah Despres, minority counsel; Josh Sharfstein, minority professional staff member; Earley Green, minority chief clerk; Jean Gosa, minority assistant clerk; and Cecelia Morton, minority office manager.

Chairman TOM DAVIS. Good morning. A quorum being present, the committee will come to order. I want to welcome everybody to today's oversight hearing on our public health system's response capabilities to manage a pandemic of contagious disease.

This year's flu season has raised the urgent question of whether our country is prepared to deal with a pandemic, be it a naturally occurring pandemic or one that results from a bioterrorist attack. Today we will examine what actions and planning procedures have been taken by Federal, State and local health officials to handle this year's flu season and other communicable disease outbreaks. Only then can we determine the potential needs of government and health officials to respond effectively to all types of contagious disease threats.

Although this year's flu season was not a large-scale epidemic, several thousand people have died from complications of the flu. Additionally, several thousand people were unable to be vaccinated due to limitations of the vaccine supply. While the flu virus is airborne and spreads easily, vaccination significantly decreases the risk of illness and helps prevent the spread of the flu virus.

Preparing for the annual flu season highlights the importance of strong cooperation between different health agencies and private

sector companies at all levels. We need to ensure that adequate production capacities for flu vaccine manufacturers exist in order to avoid a vaccine shortage next year. Once a flu pandemic is identified, it is important to determine what the public and private sector capabilities are to produce, distribute and administer diagnostics, vaccines, and drugs for this problem. This year's vaccine shortage begs the question: "Are new mechanisms and incentives needed to guarantee that effective and safe drugs, vaccines, and diagnostics can be produced as quickly as possible?"

The current influenza season has challenged our public health system's capabilities and provides us with a chance to evaluate existing procedures and safeguards. The Public Health Security and Bioterrorism Preparedness in Response Act of 2001 provided substantial new fundings for States, localities, and hospitals to boost preparedness to respond to a highly contagious disease, including influenza. The legislation included new grant programs, educational efforts, State planning requirements, expansion of Federal disaster teams, pandemic preparedness resources, and new authority to deal with public health emergencies. We will take a look at how these programs are being implemented and if funds are being allocated properly.

I understand some of our witnesses this morning will express concerns about the actual preparedness levels and Federal funding for States and localities. I look forward to a constructive dialog on those concerns. I know we all share the same goal at the end of the day: a public health system prepared to deal with an outbreak of a deadly and contagious disease.

The threat of a public health disaster emphasizes the need for planning and practice. The quicker the health community responds, the quicker a prevention and control strategy can be developed, and appropriate treatments can be identified. This hearing will recognize if any deficiencies in coordination, communication, and capacities exist and will facilitate discussions of how to work toward improvements necessary for more effective preparedness. In order to be adequately prepared, we should always be expecting the unexpected.

We have a great selection of witnesses today. I want to thank all of them for appearing with us, and I look forward to their testimony.

[The prepared statement of Chairman Tom Davis follows:]

Statement of Chairman Tom Davis
Committee on Government Reform Hearing
"A Review of This Year's Flu Season:
Does Our Public Health System Need a Shot in the Arm?"
February 12, 2004

Good morning. I want to welcome everyone to today's oversight hearing on our public health system's response capabilities to manage a pandemic of a contagious disease. This year's flu season has raised the urgent question of whether our country is prepared to deal with a pandemic, be it a naturally occurring pandemic or one that results from a bioterrorist attack. Today we will examine what actions and planning procedures have been taken by federal, state, and local health officials to handle this year's flu season and other communicable disease outbreaks. Only then can we determine the potential needs of government and health officials to respond effectively to all types of contagious disease threats.

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Preparing for the annual flu season highlights the importance of strong cooperation between different health agencies and private sector companies at all levels. We need to ensure that adequate production capacities for flu vaccine manufacturers exist in order to avoid a vaccine shortage next year. Once a flu pandemic is identified, it is important to determine what the private and public sectors' capabilities are to produce, distribute, and administer diagnostics, vaccines, and drugs for this problem. This year's vaccine shortage begs the question: are new mechanisms and incentives needed to guarantee that effective and safe drugs, vaccines, and diagnostics can be produced as quickly as possible?

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We have a great selection of witnesses to provide testimony this morning. Dr. Julie Gerberding and Dr. Anthony Fauci will discuss efforts being taken at the federal level to respond to the influenza virus. They will also describe preparedness coordination efforts with state and local authorities. Dr. Janet Heinrich, Director of Public Health Issues for GAO, will discuss the GAO report that was released this week regarding state and local preparedness in the event of a bioterrorism attack.

Joining us on our second panel will be Dr. Robert Stroube, the Virginia State Health Commissioner. He will be testifying today on behalf of the Association of State and Territorial Health Officials to provide an assessment of state and local public health departments' ability to respond adequately to a public health threat. Ms. Karen Miller from the National Association of Counties will provide the perspective from county and local health officials on preparedness. We also invited the three flu vaccine manufacturers to discuss vaccine production capacities and pandemic planning. Mr. Howard Pien, President and CEO of the Chiron Corporation and Dr. James Young, President of Research and Development at Medimmune, will be joining us. Unfortunately, a representative from Aventis Pasteur was unable to attend this hearing but the company has submitted written testimony for the hearing record. And finally, Dr. Shelley Hearne, Executive Director of Trust for America's Health, produced a noteworthy report that provided an assessment of improvements to the public health system and remaining vulnerabilities. We welcome all the witnesses and their testimony today.

Chairman TOM DAVIS. I will now yield to Mr. Waxman for an opening statement.

But let me say before Mr. Waxman, we have the D.C. Young Suffragists here to watch the hearing today, over here to our side, and let me thank all of our young people here today. Thank you for being with us.

Mr. WAXMAN. Thank you, Mr. Chairman. Let me start by thanking you for calling this hearing today. I especially appreciate your interest in public health at this relatively quiet moment—before the next crisis comes.

Public health issues either dominate the news—think of SARS and anthrax and monkeypox—or it is woefully ignored. Hearings like this one provide an important opportunity to take a step back and assess how far we have come in supporting our public health system and what more needs to be done.

We know that there will be another public health crisis, and many experts believe that this next crisis could be a global flu pandemic. In a regular flu season, about 36,000 Americans die from the flu. A pandemic could be far worse. The flu pandemic of 1918 cost millions of lives around the world, including about 500,000 in the United States. The next flu pandemic could be right around the corner. If the "bird flu" virus in Asia acquires the capacity to spread rapidly from human to human, we could be facing a pandemic.

This year's flu season exposed some of the weaknesses in our public health system. As reports of deaths among children mounted, demand for flu shots spiked. Because the demand exceeded supply, the country faced a potentially very dangerous vaccine shortage. This frightening situation led many to ask why the supply was inadequate to meet the demand.

The answer is revealing. Public health authorities recommend that about 185 million Americans get the flu vaccine every year. However, vaccine manufacturers make only about half this amount because they estimate, correctly, that only a fraction of those who should get the vaccine will actually do so.

The implications of this situation are sobering. Without an increase in demand, companies may not develop and sustain the capacity to produce sufficient quantities of a life-saving vaccine against a pandemic strain.

The solution is not to wait for a pandemic to hit. We need to increase the use of the flu vaccine each year and to enhance the role of the Federal Government in assuring manufacturers that there will be a growing market for their vaccines.

I am concerned, however, that the President's fiscal year 2005 budget undercuts flu vaccination efforts. Today, the State health commissioner in Virginia will testify that the President's budget does not include adequate funding to cover flu shots for children. His testimony is that, if adopted, this budget "will damage immunization efforts."

Today is also an opportunity to take stock of our overall public health readiness. In the wake of the attacks of September 11, 2001, and the increased concern about the threat of bioterrorism, Congress has appropriated several billion dollars to State and local public health efforts. This funding led to some improvements, such

as in the area of emergency communication. However, there continue to be major gaps.

For example, there are gaps in planning. The nonpartisan Trust for America's Health reported in December 2003 that only a quarter of the States have flu pandemic plans. The General Accounting Office will testify today that not a single State has a plan for hospital response to an epidemic involving at least 500 patients—only 500 patients.

There are also gaps in lab preparedness. In June 2003, the Trust for America's Health released a report finding that public health laboratories are "dangerously unprepared for an attack using chemicals as weapons." We will hear additional testimony today about gaps in training, education and emergency response.

At this key moment, the Federal Government's commitment to public health is essential. Investing in public health protects not only against a flu pandemic, but also against a new infectious disease and potential bioterrorist threats.

Unfortunately, the President's budget is again a major disappointment. While it extends tax cuts for the richest Americans, this budget cuts CDC funding 3 percent and reduces the amount of money going to State and local governments for public health readiness by over $100 million.

The President has assured the American people that he is doing everything possible to protect them. His public health budget indicates otherwise. This is a budget that does not take advantage of this brief respite between public health crises to prepare adequately for the next one.

Congress needs to be sure that the budget it passes does not make the same mistakes.

I thank the witnesses for appearing today. I look forward to their testimony.

I thank you again, Mr. Chairman, for convening this important hearing.

[The prepared statement of Hon. Henry A. Waxman follows:]

Opening Statement of
Rep. Henry A. Waxman, Ranking Minority Member
Committee on Government Reform
Hearing on
"A Review of This Year's Flu Season: Does Our Public Health System Need a Shot in the Arm?"
February 12, 2004

Let me start by thanking Chairman Davis for calling this hearing today. I especially appreciate his interest in public health at this relatively quiet moment—before the next crisis comes.

Public health either dominates the news—think of SARS and anthrax and monkeypox—or it is woefully ignored. Hearings like this one provide an important opportunity to take a step back and assess how far we have come in supporting our public health system and what more needs to be done.

We know that there *will* be another public health crisis. And many experts believe that this next crisis could be a global flu pandemic. In a regular flu season, about 36,000 Americans die from the flu. A pandemic could be far worse. The flu pandemic of 1918 cost millions of lives around the world, including about 500,000 in the United States. The next flu pandemic could be right around the corner. If the "bird flu"

virus in Asia acquires the capacity to spread rapidly from human to human, we could be facing a pandemic.

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Congress needs to be sure that the budget it passes does not the same mistake.

I thank the witnesses for appearing today and I look forward to their testimony.

Chairman TOM DAVIS. Thank you.

Are there any other Members that wish to make opening statements? Hearing and seeing none, we now move to our first panel of witnesses.

We have Dr. Julie Gerberding and Dr. Anthony Fauci, who will discuss efforts being taken at the Federal level to respond to the influenza virus. They will also describe preparedness coordination efforts with State and local authorities. Dr. Janet Heinrich, the Director of Public Health Issues for GAO, will discuss the GAO report that was released this week regarding State and local preparedness in the event of a bioterrorism attack.

It is the policy of the committee that all witnesses be sworn, so if you would rise with me and raise your right hands.

[Witnesses sworn.]

Chairman TOM DAVIS. Be seated. I think we have been through the rules. We have a light in front of you. It turns orange after 4 minutes, red after 5 minutes. Try to sum up in that time. Your total statement is already in the record, and questions will be based on the total statement.

Dr. Gerberding, we will start with you and move down the way, and thank you very much for being with us.

STATEMENTS OF DR. JULIE GERBERDING, DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION; DR. ANTHONY S. FAUCI, DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES; AND DR. JANET HEINRICH, DIRECTOR, PUBLIC HEALTH ISSUES, GENERAL ACCOUNTING OFFICE

Dr. GERBERDING. Thank you, Mr. Chairman, members of the committee, for allowing me to be here today. What I would like to do is to frame the discussion about preparedness and why we need to be prepared for influenza by pointing out the picture of this year's outbreak investigation status.

[Slide shown.]

Dr. GERBERDING. You can see in the first graphic here what the United States looked like in October when a single State, Texas, was reporting significant localized influenza activity. In just a few weeks, all of the red States were showing widespread activity. And by the end of December, almost the entire United States was involved in a very large-scale flu outbreak. Fortunately, as of the end of January, most of the States now are just showing sporadic or very localized activity.

But this was a flu season that started much earlier than we have ever seen, spread faster, and in no time in our history of surveillance have we ever seen that much widespread activity across the United States at a single point in time. So it was a wake-up call. Fortunately, it turned out to be not the worst epidemic we have had, but a warning sign that further preparedness efforts clearly are necessary. And I certainly appreciate Mr. Waxman's remarks about the impending possibility of a pandemic.

[Slide shown.]

Dr. GERBERDING. On the next graphic I have depicted the 1918 flu outbreak and its impact on mortality in the United States at the beginning of the last century, just to point out what an extraor-

dinary capability flu does have. This is a deadly virus, and it is a tricky virus, because it is constantly undergoing evolution, and that is why we need to get a new flu shot every year. Usually the evolution is in minor steps, so the vaccine in 1 year looks pretty much like the vaccine in the past year. But occasionally we see very large-scale changes in the virus, and that is really what traditionally has set off a pandemic.

[Slide shown.]

Dr. GERBERDING. On the next graphic I have mapped out over time how viruses move from animals to humans and create these pandemic strains. There are 15 types of flu virus. They are all present in migratory birds like ducks. These avian viruses are present in nature in ducks; they usually don't cause disease. Occasionally they move to other species like chickens, and some of them cause very severe bird flu disease in chickens like we are seeing in Asia right now.

Human viruses and bird viruses can mix up in pigs, because pigs are vulnerable to both infections. And sometimes when this happens their genes get mixed up so a brand new, very novel flu strain evolves. This is called a re-assorted virus, and when that virus enters the human population, we have never seen it before, none of us have immunity to it, and a pandemic can occur. This has been our concern all along, because this happens periodically, as I will show you in a moment.

But recently we have also begun to be very concerned about the possibility of these avian viruses directly moving to people and then evolving in people to become much more efficient in their transmission from person to person. That has never happened, but biologically it is plausible, given how these viruses evolve.

So we have two mechanisms where we could end up with a novel strain of a virus that could set off a pandemic.

[Slide shown.]

Dr. GERBERDING. On the next graphic I have mapped out over the past century how pandemics in the United States occurred. The 1918 virus was an H1 virus, and that caused the very large spike in mortality that I demonstrated. In 1957 a brand new virus appeared, an H2 virus, that set off the Asian flu pandemic. In 1968 the Hong Kong H3 virus first appeared and set off that pandemic. H1 came back a few years later, it did not cause a pandemic in people over age 20 because they had some immunity from the old outbreak, but it did cause a very large outbreak among people under age 20.

Today we generally have circulating H1 virus, H3 virus, and influenza B virus in the human population. That is why our vaccine has to contain three different strains of virus in order to protect us from what is currently common in our population.

But up here at the top of the graph I have shown also the little clusters of bird flu that have emerged and been transmitted to people over the last several years. This has happened sporadically before, but since 1997 it has been happening with a regular frequency. And it is these bird flu strains that, of course, have our attention right now as their potential for evolving and becoming more efficiently transmitted in humans.

[Slide shown.]

Dr. GERBERDING. On the next graphic I have just provided a brief overview of the timeline for vaccine development, because it is really this timeline that has caused the biggest challenge in preparation for pandemic flu. As you pointed out, there are 185 million people in this country who need flu vaccine. What CDC does in conjunction with WHO and investigators around the world is constantly sample viruses, genetically characterize them in our research labs, and anticipate what might be the next strain.

When we see a new virus pop up, we work with it in the laboratory with our colleagues in St. Jude's in Tennessee and in a laboratory in the United Kingdom to try to create the best possible virus for vaccine. But that takes time, and we have to get a virus that is safe enough to work with and is able to be propagated well in eggs, since that is the methodology we are using. The best possible timeframe from getting the virus and getting it into a form for vaccination is about 4 months, and that is a best case scenario.

So we are constantly operating under this very narrow window of opportunity to get the right virus, manipulate it genetically to be suitable for vaccination, and then produce the vaccine that we need. And we are doing this right now in an egg base culture system, which is a very old fashioned way of making vaccine, and I think it speaks to the other challenge in all of this, which is basically the capacity of our manufacturers to utilize this technology in a fast enough timeframe to get what we need done.

So the three challenges that Secretary Thompson has asked us to address at NIH, CDC, FDA, and the other departmental agencies as we prepare the Department's pandemic planning are: No. 1, how are we going to get those 185 million people vaccinated; No. 2, how are we doing to get enough vaccine to assure that we have the supply we need when we need it; and, third, how are we going to modernize our vaccine production so that we can get the job done.

Thank you.

[The prepared statement of Dr. Gerberding follows:]

Testimony
Before the Committee on Government Reform
United States House of Representatives

Protecting the Public's Health: CDC Influenza Preparedness Efforts

Statement of
Julie L. Gerberding, M.D., M.P.H.
Director
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services

CDC
SAFER • HEALTHIER • PEOPLE™

For Release on Delivery
Expected at 10:00AM
on Thursday, February 12, 2004

Good Morning, Mr. Chairman, Members of the Committee. Thank you for inviting me here today to provide information regarding the current influenza season and the country's preparedness for a major public health threat. Assuring the Nation's preparedness has been one of Secretary Tommy Thompson's greatest priorities.

Introduction

As you are aware, this influenza season presented several challenges for the nation's public health system. The season began and peaked earlier than in most years; there was substantial media coverage, particularly of disease and death among children, creating the perception that the season was more severe than prior years and demand for trivalent inactivated influenza vaccine exceeded the amount that had been produced by the market. There were other complications this season, as well, revolving around reports of a more severe season than usual being caused by an H3N2 strain of influenza, which is often associated with more severe influenza seasons, and surveillance data showing that the predominant virus circulating was different from the corresponding strain contained in the vaccine. I will outline what the Centers for Disease Control and Prevention (CDC) did to respond to this situation and provide information on the current state of preparedness for a larger scale event. The timing of this hearing is opportune, as CDC is very concerned about the recent widespread outbreaks of avian influenza in poultry flocks spanning many countries in Asia and the associated human illnesses and deaths reported from Thailand and Vietnam.

The situation of limited availability of influenza vaccine this year arose from the unusual combination of: (1) an early onset of relatively severe influenza which led to a surge in demand for the vaccine at the end of the traditional vaccination season; and, (2)

production of the same number of doses of trivalent inactivated influenza used in prior years which was not adequate to meet the surge in demand that occurred this past influenza season. The surge in the demand for vaccine was also sparked by the reporting of substantial numbers of pediatric cases of influenza, including severe or unusual complications and deaths, noted in several states. At this point, it is unclear whether influenza is impacting children more severely than in other years or if a heightened awareness of severe influenza disease in children has led to increased testing and reporting of pediatric cases. The overall influenza morbidity reported from surveillance this influenza season is similar to what has been seen in other years where an H3N2 influenza strain predominated.

While our experience this influenza season has heightened national interest in influenza disease and its prevention, CDC has long recognized the impact of this disease on our population and its importance as a cause of illness, hospitalization, and death. CDC scientist's estimate that an average of 36,000 people die from influenza-related complications each year in the United States. At a meeting of the National Vaccine Advisory Committee (NVAC) last week, Dr. Christina Beato, Acting Assistant Secretary for Health, called on the committee to work with CDC and other Department of Health and Human Services (DHHS) agencies to review the entire influenza vaccination system and make recommendations on how we can improve our prevention efforts. We welcome this charge and will work with NVAC to provide a preliminary report to the Assistant Secretary in June. The Department has, however, already begun important new vaccine development activities, which I will describe later in this testimony.

Vaccinating individuals who are at greatest risk of serious complications from influenza is the primary strategy for preventing severe complications from the disease, including

associated deaths. Our communications to the public urging them to get vaccinated as the most effective means of prevention has helped yield the strong consumer demand for influenza vaccine this year, exceeded the demand seen in previous influenza seasons. Some healthcare providers used all of their supplies of influenza vaccine. In past years, supply has generally been sufficient to meet demand. Typically, almost all influenza vaccination is completed by late November. This year, however, a surge in demand began in late November continuing into the month of December. At a time when influenza vaccination clinics are typically winding down, people were still seeking vaccination.

Communications 2003-2004 Influenza Season

Each year, CDC works with the Advisory Committee on Immunization Practices (ACIP) to review and update influenza vaccination recommendations. These annual recommendations are published before each influenza season so that providers can become familiar with these recommendations and have time to implement any recommended changes. Prior to the influenza season CDC conducted its annual national public-education campaign to promote the benefits of influenza vaccine and the most current influenza vaccination recommendations. Partnerships with health departments, medical societies, social service organizations and the private sector were important elements in the influenza communication efforts. Based on formative research, printed materials were developed in both English and Spanish and made available on the website. A national media campaign, consisting of press conferences, teleconferences, new releases (video, audio and print) was launched in September.

As I have stated, the influenza season started early this year. In October, CDC received reports about several laboratory-confirmed school outbreaks in Texas. Preliminary analysis of the Texas isolates at CDC showed that some were different from the strain contained in the vaccine for the current year. CDC increased its efforts to analyze the viruses circulating in the United States as quickly as possible and to educate our partners and the public about this season's vaccine and the need for timely vaccination. A series of CDC Health Updates, Morbidity and Mortality Weekly Reports (MMWR) and additional guidelines for infection control and use of influenza antiviral drugs were disseminated by CDC to keep health care providers and states informed of important information as the season progressed.

Production of influenza vaccines is a complex process that requires many steps, including selection of suitable vaccine viruses, growth of these viruses in eggs, and testing to ensure safety and purity of the vaccine. Recommendations about which strains should go into the vaccines for the United States are based on year-round surveillance and are typically made in February for vaccine that will be used in the following season. The A/Fujian strain was identified late in January 2003. At that time, it seemed possible that this strain might predominate during the coming influenza season, but it was too early to be certain. In addition, there was no isolate that had been grown exclusively in eggs. Currently all influenza viruses used in vaccine production are grown only in eggs or avian cell culture.

U.S. health authorities postponed their recommendation about which A (H3N2) strain should be included in the vaccine for a full month (until March) while more viruses were tested and while attempts were made to grow an egg isolate of the A/Fujian virus that could be used in vaccine production. A suitable isolate could not be grown in time and

waiting longer likely would have jeopardized the supply of influenza vaccine for the 2003-04 season. Because of these considerations, in March it was recommended that the influenza vaccine for the 2003-04 influenza season include an A/Panama strain, which is related to the A/Fujian strain. This chain of events is a reminder of the fragility of a time-consuming vaccine production process that is reliant upon eggs. The Department is undertaking efforts to move toward the development of a modern, cell culture influenza vaccine, for which production can be scaled up more rapidly than the traditional egg-based vaccine.

Childhood influenza has been of concern to CDC for the past several years and was highlighted this year in the media. A CDC study showed that children less than two years of age were at a similar risk for hospitalization due to influenza complications as older age groups for which vaccine is recommended. The ACIP voted in October 2003 to recommend routine use of influenza vaccine for children 6-23 months of age, beginning in the 2004-2005 influenza season. Previously, influenza vaccine had been encouraged for this age group but no formal recommendation had been made. CDC also has been closely following reports from Japan about influenza-related pediatric encephalopathy cases and has increased our own efforts to report and characterize severe disease in the pediatric populations. This season CDC sent additional requests to all state health departments to report cases of influenza related deaths in the pediatric populations. Discussions are underway with state and national partners about the feasibility of making the reporting of influenza deaths in pediatric populations nationally notifiable. CDC continues to analyze pediatric mortality data collected this year. The attention that this topic has received is timely in that it underscores the severe impact influenza has on pediatric populations, particularly for children with chronic medical conditions.

As the season progressed and widespread disease was reported in virtually every State, CDC activated its Emergency Operations Center (EOC) on December 5, 2003. This enabled CDC to respond to the multiple issues surrounding vaccine supplies, to enhance efforts to document morbidity and mortality caused by influenza, and to develop additional guidelines for the prevention or treatment of influenza. A focus was placed on providing frequent, up-to-date guidance to state public health partners, health care professionals and the general public about how and where to obtain vaccine and how to prevent and control influenza.

Vaccine Supply 2003-2004 Influenza Season

The situation of limited availability of influenza vaccine this year arose from the unusual combination of an early onset of severe influenza outbreaks leading to a surge in demand for the vaccine later than usual in the influenza season and production of the same doses of the influenza vaccine used in previous years which was not adequate to meet the surge in demand. Addressing issues associated with the increased demand for influenza vaccine this season was a major focus of CDC actions.

U.S. licensed influenza vaccine is produced by three manufacturers--two making inactivated vaccine and one making a live attenuated vaccine delivered by nasal spray. All vaccine is produced, and the vast majority distributed, by the private sector. Because of the time required to manufacture vaccine and the need to obtain adequate supplies of embryonated eggs in which influenza virus is grown for vaccine production, manufacturers must predict demand and decide on the number of vaccine doses to produce approximately 6 to 9 months before onset of the influenza season. For the

2002-2003 influenza season, manufacturers produced approximately 95 million doses of influenza vaccine of which about 83 millions doses were used; and the remaining 12 mission doses that were produced went unused. Production of vaccine for this year was based on last year's demand--manufacturers produced about 83 million doses of the inactivated vaccine, as well as about 4 million doses of the new live vaccine, FluMist, for a total of about 87 million vaccine doses.

CDC vaccine recommendations are made through a deliberative process involving advice and guidance from the ACIP. The ACIP issues recommendations regarding influenza vaccination, including which groups of individuals are at highest risk for developing complications from influenza, and optimal time frames for administering vaccine. If vaccine manufacturers delay production, or if there is a shortage of influenza vaccine, CDC can take steps to minimize the effects.

Actions Taken By CDC 2003-2004 Influenza Season

CDC took aggressive steps to communicate issues regarding influenza to all possible audiences. As a first step, the CDC influenza website was completely reorganized. A single site with all influenza related information made information easier to find. A series of updates targeted at all audiences were prepared and posted to inform providers and the public of the latest information on vaccine availability, guidelines for the prevention and control of influenza and answers to the many questions that arose as the influenza season progressed. A proactive campaign to keep health care providers and states informed as the season progressed was also mounted through the dissemination of a series of CDC Health Updates and MMWRs reports beginning October 20, 2003. These publications provided updates on U.S. influenza activity and

addressed issues such as the importance of timely vaccination, with priority placed on vaccinating persons at high risk for complications from influenza, including children 6-23 months of age; interim guidelines on the use of antiviral medications for prophylaxis and treatment; and, the request for reporting of severe pediatric cases through state public health departments.

Actions taken by CDC in response to the demand for influenza vaccine this season include the following:

- CDC worked with the vaccine manufacturers, distributors, health care providers, and state and local public health departments to redistribute vaccine wherever possible from areas with vaccine excess to those with the greatest need.

- CDC also explored every opportunity to obtain additional doses of influenza vaccine. In December and January, we were able, through the contracting process to obtain 463,000 doses of adult influenza vaccine, and 213,000 of the pediatric doses. Additionally, 49,000 doses of FluMist were donated by the manufacturer and more than 40,000 doses of inactivated vaccine were received from the Department of Veterans' Affairs. The principal consideration in allocating these additional doses was to distribute them in a fair and equitable manner to reach as many high-risk individuals as possible.

- CDC encouraged states to develop plans to help manage and direct vaccine supplies in their jurisdictions.

- The CDC Emergency Operations Center was activated.

- Special calls were held with National Influenza Vaccine Summit participants and with partners. The National Influenza Vaccine Summit, co-chaired by the American Medical Association and CDC, consists of organizations dedicated to improving influenza control.

- Several studies were begun at CDC to obtain rapid assessments of the effectiveness of this year's vaccine. Work on these studies is ongoing. It is difficult to implement these studies in the middle of the influenza season and we need to develop a routine system for real time measurement of how well influenza vaccines are protecting our citizens.

- The National Vaccine Program Office (NVPO) in the Department of Health and Human Services has responsibility for coordinating and ensuring collaboration among the many federal agencies involved in vaccine and immunization activities. As such, they are completing a pandemic influenza preparedness and response plan that will include approaches for improving annual influenza disease control, including vaccine production, distribution, and administration.

Preparedness for Communicable Disease Outbreaks Including Influenza

This year's influenza season and the threat of an influenza pandemic, exemplified by the current situation with avian and human deaths in Asia caused by H5N1 viruses,

highlight the importance of improving the nation's preparedness to respond to disease outbreaks such as influenza. Much work has been done to improve the public health infrastructure during recent public health emergencies. Our current and evolving efforts include: (1) expanding our capacity to conduct surveillance for influenza to try to identify new strains of influenza more rapidly so that they can be incorporated in vaccines; (2) conducting research that leads to the development of better vaccines and vaccine candidates for use during annual influenza outbreaks and in a pandemic; (3) improving the nation's vaccine supply to meet demand and eventually cover the 185 million American for whom influenza vaccine is recommended; (4) improving the infrastructure needed to deliver vaccines; (5) developing stockpiles of antiviral drugs and other medications and items that will be in short supply during a pandemic; (6) developing communications strategies and materials; (7) improving coordination with and planning by our state, local and private sector partners; and, (8) We also need to assure that more of our health care providers receive influenza vaccine. According to the National Health Interview Survey for Health Care Workers, only 36 percent to 41 percent of health care providers receive influenza vaccine annually.

In a time when U.S. and international health are inextricably linked, the fulfillment of CDC's domestic mission – to protect the health of the US population – requires increased global awareness and collaborations with global partners. Beginning in FY 2004, CDC is investing in a Global Disease Detection initiative, which will facilitate the faster recognition of infectious disease outbreaks globally, improved ability to control and prevent outbreaks, and enhanced capability to detect emerging microbial threats. By expanding international surveillance network and filling gaps in key areas of the world, we will gain greater access to circulating influenza viruses from other parts of the world. By increasing the international partners who regularly share influenza virus

isolates through the World Health Organization (WHO) surveillance network, we will increase our ability to detect new variants earlier, and thus be in a better position to make vaccine decisions. At the same time we will have the added benefit of detecting new viruses with pandemic potential and for other infectious diseases. The surveillance network created for influenza played a key role in detecting and characterizing the spread of SARS. Enhancements also are needed for domestic surveillance. These include improving the ability of state public health laboratories to detect and subtype influenza viruses, expanding the sentinel provider surveillance system, and developing a new system of reporting for hospitalizations associated with influenza. This hospital-based information is crucial for understanding the impact of influenza on both people and the health care systems that treat them.

There are several ways by which prevention of influenza by vaccination can be improved. More information needs to be collected about the effectiveness of influenza vaccines to determine the impact of vaccine in various populations for whom vaccine is recommended in reducing the burden of influenza and to help in evaluating whether the present strategy which is focused on vaccination of person at high risk of influenza is the most effective way to reduce the burden of this disease. For example, more vaccination of healthy younger people may lead to indirect protection of high risk persons, by reducing the likelihood that such persons will be exposed to the virus. Additionally, research is needed to better understand the immune response to influenza vaccines--particularly among high risk groups such as the elderly--and to improve influenza vaccines so that they are more effective in preventing disease and death. This research is underway. Finally, there are several approaches that can be pursued to expand influenza vaccine supply and availability at the time of a pandemic.

DHHS is currently beginning work on long-range strategies to improve influenza vaccine supple in the future. The current egg-based system used to produce licensed influenza vaccines – despite being reliable for more than 40 years – can be improved. Limitations of the current system include: 1) a lengthy manufacturing process; 2) the need to select which virus strains will be in the vaccine at least six months in advance of the influenza season; 3) the need to produce nearly 90 million doses of a new influenza vaccine each year; and 4) the requirement of hundreds of millions of fertilized chicken eggs to manufacture the vaccine. The current production techniques to make influenza vaccine cannot be scaled up rapidly to provide additional doses of vaccine in a bad influenza season or in the event of an influenza pandemic. In the 2003-2004 season, the national demand for vaccine was higher than the 87 million doses that were produced for the United States. In the event of an influenza pandemic, the demand for =vaccine could spike to between 280 million and 575 million doses, with no more than four or five months for manufacturing – and it would have to be made in the U.S. to ensure its availability. DHHS is encouraging the development and U.S. licensure of influenza vaccines produced using new technology, including the development of cell-based vaccines. Given that industry generally produces enough annual influenza vaccine to meet demand under the current egg-based production methods, they would not get a return on the investment that would be needed to switch to a cell culture method of production. Resources have been made available in the FY 2004 budget, and requested in the FY 2005 budget, for this activity. We are very grateful that $40 million dollars was allocated for the pediatric influenza vaccine stockpile in the recently passed budget. Additionally, the President's fiscal year 2004 budget request included $100 million for pandemic preparedness and Congress appropriated $50 million. The President's fiscal year 2005 request again includes $100 million for pandemic preparedness.

As part of CDC planning efforts, we also have been evaluating approaches with vaccine manufacturers for increasing annual vaccine production. One important stimulus to increased production is increased demand and annual vaccine use. Through our educational efforts for providers and the public, we are stimulating increased vaccination. To achieve our Healthy People 2010 targets of vaccinating 90 percent of adults 65 years and older and 60 percent of high-risk adults ages 18 to 64, we will need to increase these efforts and to address other barriers to vaccination. CDC participates on international workgroups to develop guidance for the production and licensing of vaccines using new technology such as reverse genetics and participates internationally in efforts to look at global vaccine supply issues.

CDC has been working with the private sector, state and local health officials and provider organizations in the development of contingency plans and is taking steps to help ensure that high-risk patients are vaccinated in the event of a delay or shortage. Several activities are underway and are planned to anticipate and deal with potential problems.

- CDC has continued its collaboration with the Centers for Medicare and Medicaid Services (CMS) to encourage and promote "standing orders" to improve influenza and pneumoccocal vaccination levels in nursing homes throughout the country. A standing order enables nursing homes to provide these vaccinations to nursing home residents without an individual prescription. In 2002, CDC and CMS completed a three year program to promote standing orders for Medicare patients in nursing homes. Initial data showed that standing orders are both more effective and more cost-effective than other methods for increasing immunization rates in

increasing immunization coverage against influenza and pneumoccocal diseases among nursing home residents.

- In addition, Medicare increased its reimbursement rates to health care providers to deliver vaccine to their patients. The Medicare reimbursement rate for administration of flu vaccine increased from an average of $3.98 in 2002 to $7.72 in 2003 – an increase of 94 percent. The reimbursement rate for the vaccine product also increased, from $8.02 to $9.95.

- CDC and the American Medical Association hosted a National Influenza Vaccine Summit for the past three years with manufacturers, selected distributors, trade organizations, provider organizations and public health officials to learn more about private sector production and distribution challenges and to address contingency planning.

- In July 2001, CDC implemented the DHHS Racial and Ethnic Adult Disparities in Immunization Initiative (READII) in five demonstration sites to improve influenza and pneumoccocal vaccination rates for African-Americans and Hispanics 65 years of age and older. This initiative is being implemented with the support of the CMS, HRSA, the Administration on Aging, the Agency for Healthcare Research and Quality (AHRQ), and other federal agencies.

- CDC, beginning in 2001, requested that states develop contingency plans in the event of an influenza vaccine shortage and provided written guidelines to assist them in planning. In March of 2003, 15 states had

complete or draft plans and 34 states were preparing their plans. We will get an updated status on this next month.

- CDC is evaluating strategies to improve influenza vaccine supply in the future. The recent addition of the $40 million for the VFC program to stockpile the vaccine will help us in these efforts. DHHS is completing a pandemic influenza preparedness and response plan that will include approaches for improving influenza surveillance, expanding vaccine research, and improving annual influenza disease control, through vaccine production, distribution, and administration.

- Each year, CDC encourages those for whom vaccine is recommended to receive influenza vaccines, and we will continue these efforts in the future.

Influenza antiviral drugs can have an important impact on morbidity and mortality from influenza disease and would have a role in the event of a pandemic. Studies show these drugs are 70 to 90 percent effective in preventing influenza when begun as chemoprophylaxis before exposure to influenza virus. Additionally, one class of drugs has been shown to decrease hospitalizations and lower respiratory complications such as pneumonia and bronchitis when used as treatment. In an influenza pandemic, use of antiviral drugs may be particularly important early in the response to protect and prevent transmission by persons who perform critical functions such as first responders, including health care workers, and those responsible for public safety. This season CDC acquired, with the strong support of Secretary Thompson, several hundred thousand treatment courses of one antiviral drug as part of the Strategic National

Stockpile. A range of issues including the ability of the manufacturers to supply large amounts of drug quickly, currently are being explored. Antiviral drug resistance is a concern in that it can render the more widely available and lower cost antiviral medications ineffective, as was demonstrated for the strain of avian influenza causing deaths in Vietnam and Thailand. Even more ideal than an antiviral stockpile, however, is an effective influenza vaccine.

While we are addressing the issues of surveillance, vaccine supply, and antiviral drug stockpiles at the national level and these efforts will provide the ability to respond to an influenza pandemic, actually implementing that response is the job of the state and local health departments and the health care system. Federal funding, guidelines, and technical assistance are available to support planning efforts at state and local levels. CDC also is developing tabletop and field exercises to practice those plans.

Conclusion

Mr. Chairman, our surveillance data are showing that although the influenza season arrived earlier than usual this year, the morbidity and mortality caused by influenza this year was on par with other recent years when influenza A(H3N2) viruses predominated, though unprecedented media attention helped to increase consumer demand for vaccine late in the influenza season. Normally, we have millions of doses that go unsold and get discarded. This year is unprecedented in that interest in influenza vaccination remained strong into December and all doses of inactivated influenza vaccine were sold. CDC, and its partners, took steps to make the situation better by working with the private and public sectors to obtain vaccine and assist with redistribution. The challenges caused by this year's consumer demand for vaccine

highlight the urgent need to improve the Nation's capacity to prepare for a catastrophic event of a much larger nature, as can occur in an influenza pandemic.

To address the challenges we face, we need to be able to respond to an unusually bad influenza season, or an influenza pandemic, more rapidly than current vaccine production methods allow. In addition, we need to enhance our surveillance activities so we can detect virus variants earlier so they can be incorporated into our vaccine. We must continue and strengthen our promotional efforts to educate the public about the importance of routine influenza immunization to create the demand to vaccinate high-risk individuals, alleviate surges in demand, and develop a consistent market so manufacturers can better gauge vaccine supply. The recent recommendations to vaccinate all 6-23 month old children and their household contacts will help reduce the terrible burden of pediatric morbidity and mortality. The $40 million made available in FY 2004 and FY 2005 to develop an influenza vaccine stockpile through our VFC program will help us respond to sudden unanticipated surges in demand. And our continuing collaboration with state and local health care providers, in both the public and private sectors will help to focus on preparedness efforts.

DHHS is completing a pandemic influenza preparedness and response plan that will include approaches for: improving surveillance; targeting research to improve influenza vaccines and promote the use of new vaccine production technology; and, provide surge production capacity establishing mechanisms to work with manufacturers to ensure adequate annual vaccine production; and improving coordination with public and private partners. Together we will continue to work to improve our Nation's ability to plan and prepare for a pandemic.

Thank you again for holding this hearing on such an important public health issue. I would be happy to respond to any questions you may have.

Appendix I

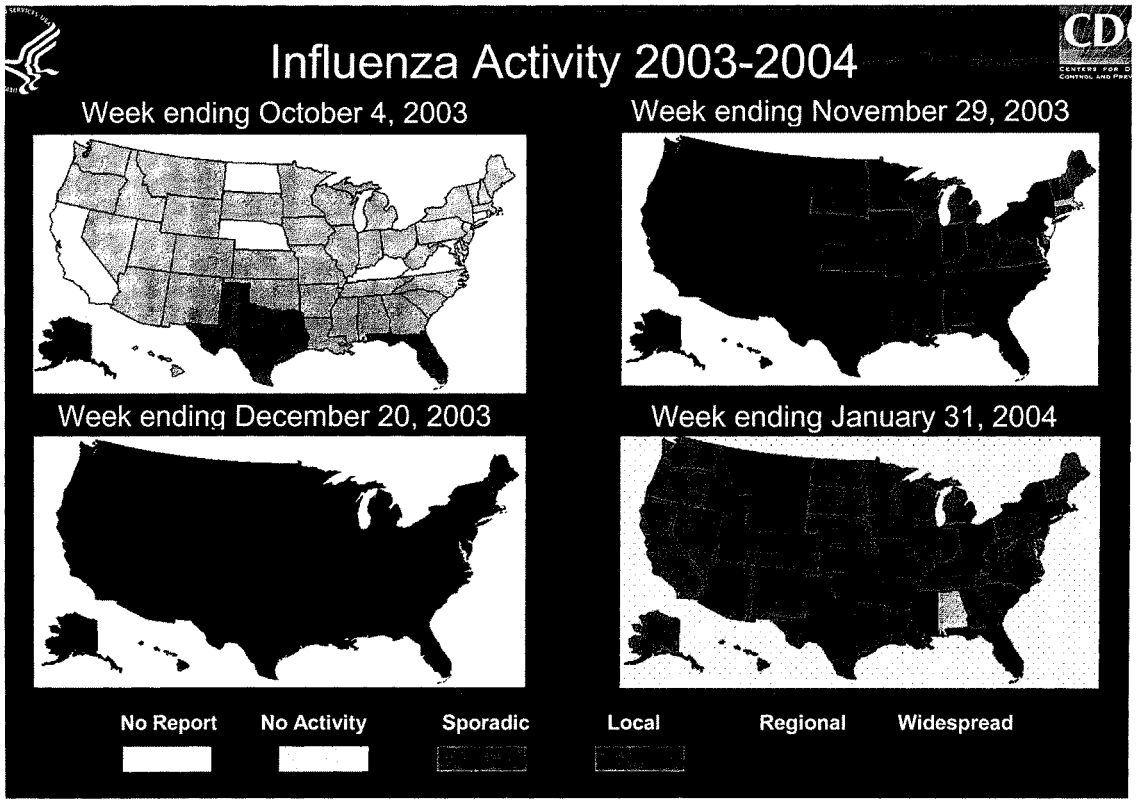
The initial recommendations made by the ACIP for the prevention and control of influenza for the 2003-2004 season were reported in CDC's April 25, 2003, Morbidity and Mortality Weekly Report (MMWR) (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5208a1.htm).

The ACIP recommends the following individuals get vaccinated against influenza:

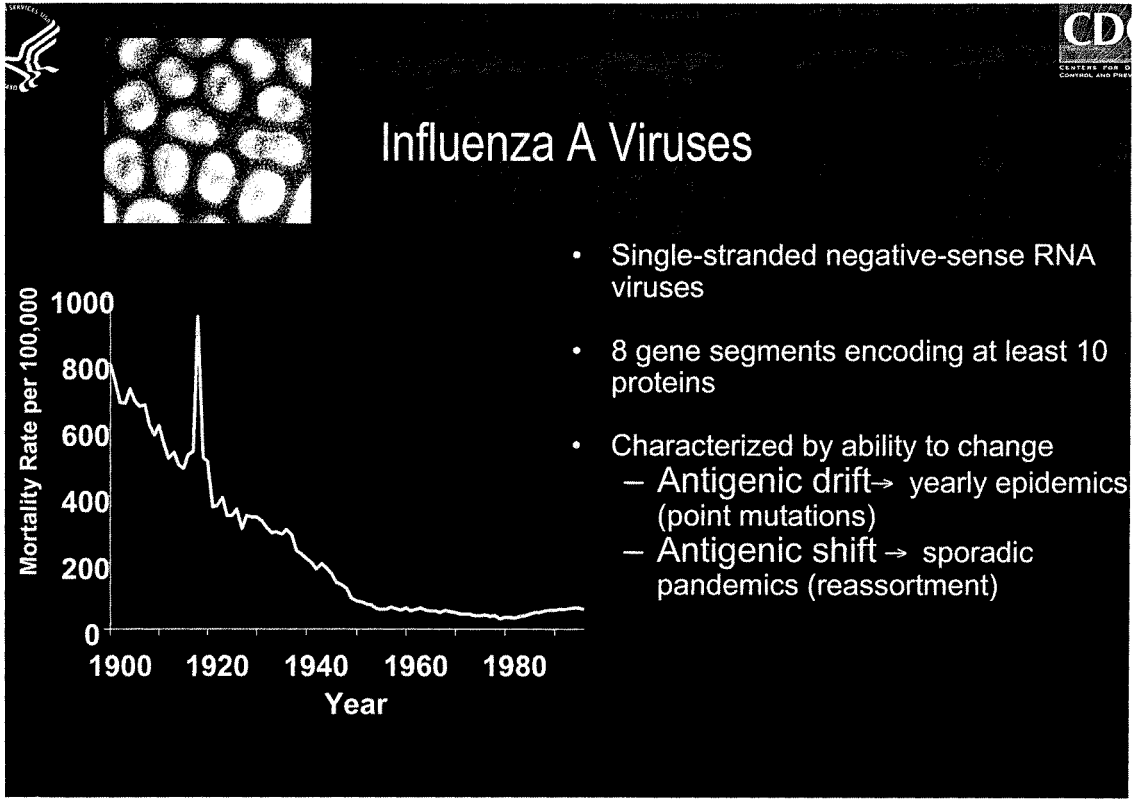
- persons 50 years and older;
- residents of nursing homes and other long-term care facilities;
- adults and children 6 months of age and older with chronic heart or lung conditions;
- adults and children 6 months of age and older who need regular medical care or had to be in a hospital because of metabolic diseases, chronic kidney disease, or a weakened immune system;
- children and teenagers 6 months to 18 years who are on long-term aspirin therapy;
- women who will be more than 3 months pregnant during the influenza season; and
- healthy children 6-23 months of age (to begin in 2004-2005 according to October 2003 recommendation of ACIP, implemented this year).

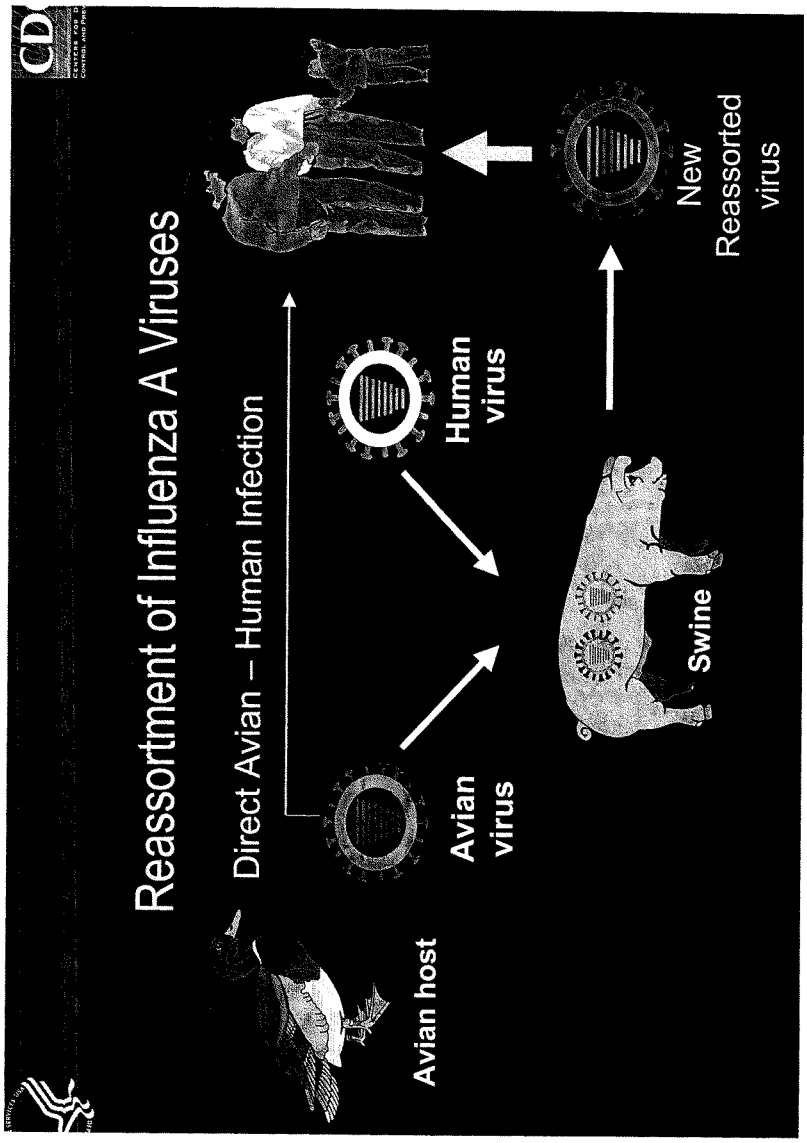
In addition, the ACIP recommends the following groups get vaccinated to prevent spread to individuals at high risk of complications from influenza:

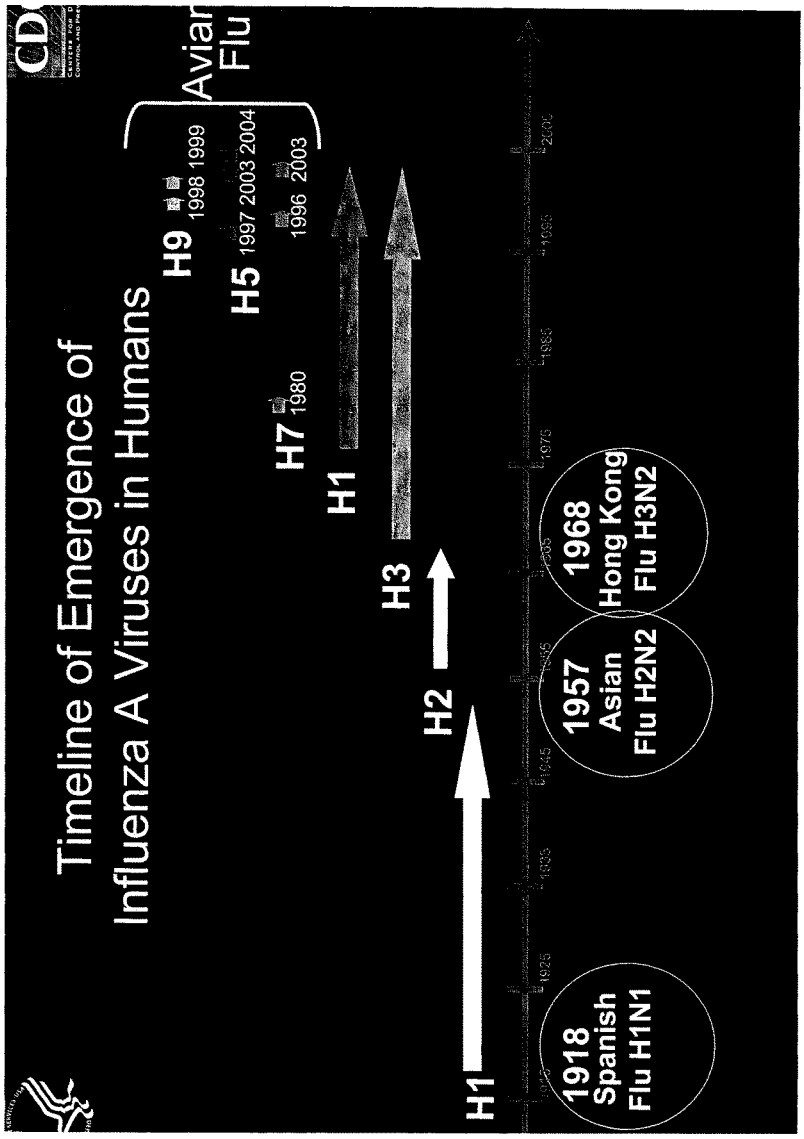
- doctors, nurses, and other employees in hospitals and doctors' offices, including emergency response workers;
- employees of nursing homes and long-term care facilities who have contact with patients or residents;
- employees of assisted living and other residences for people in high-risk groups;
- people who provide home care to those in high-risk groups; and
- household members of people in high-risk groups


Influenza Activity 2003-2004
Week ending October 4, 2003
Week ending November 29, 2003
Week ending December 20, 2003
Week ending January 31, 2004
No Report
No Activity
Sporadic
Local
Regional
Widespread

Record


Influenza A Viruses
Mortality Rate per 100,000
1000
800
600
400
200
0
1900
1920
1940
1960
1980
Year
• Single-stranded negative-sense RNA viruses
• 8 gene segments encoding at least 10 proteins
• Characterized by ability to change
– Antigenic drift→ yearly epidemics (point mutations)
– Antigenic shift → sporadic pandemics (reassortment)


Reassortment of Influenza A Viruses
Direct Avian – Human Infection
Avian host
Avian virus
Human virus
Swine
New Reassorted virus


Timeline of Emergence of
Influenza A Viruses in Humans
Avian Flu
H9 1998 1999
H5 1997 2003 2004
H7 1980
1996 2003
H1
H3
H2
H1
1918 Spanish Flu H1N1
1957 Asian Flu H2N2
1968 Hong Kong Flu H3N2

Timeline for Influenza Vaccine Development and Use
United States
STEPS
Surveillance
Select strains
Prepare reassortants
Standardize / test antigen
Review labels / license
Assign potency
Release vaccine
Produce concentrates
Formulate & test
Fill, test, package
Distribute
Vaccinate !
CDC/ WHO
FDA
Manufacturers
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec
CDC

Chairman TOM DAVIS. Thank you very much.

Dr. Fauci.

Dr. FAUCI. Thank you very much, Mr. Chairman, members of the committee. It is a pleasure to be here with you today, and thank you for giving me the opportunity to testify before this committee.

I am going to talk to you for a couple of minutes from the perspective of the biomedical research endeavor to meet the threat of emerging and re-emerging diseases in general, but specifically, for today's purposes, influenza.

[Slide shown.]

Dr. FAUCI. This particular map of the world shows just over the last 20 or so years the number of emerging and re-emerging diseases with which we have been confronted both in the United States and worldwide. When we talk about emerging diseases, we talk about brand new diseases. Some examples are HIV and SARS. A re-emerging disease is a disease that is an old disease but that reappears in a different form, in a different geographic location. We have experienced West Nile virus since 1999, which is a re-emerging disease; it has been around for a long time.

But perhaps the epitome of the continually re-emerging infection is influenza, particularly influenza A, because it has the capability of slightly changing from year to year, which necessitates our having essentially new vaccines each year, as well as the possibility and potential to do what Dr. Gerberding mentioned, about changing so dramatically that it is essentially a new virus.

[Slide shown.]

Dr. FAUCI. And the molecular reason for that is really rather simple. The influenza virus has a number of genes and proteins. The two that are used for designation are the hemagglutinin, which refers to the H, where we get the H3, H1, H2; and the neuraminidase, which is the N. We have an example this year of both a shift and a potential drift. A drift is a very slight change. Our vaccine this year had the H3N2 Panama strain. What we were confronted with was an H3N2 Fujian strain, a slight difference, not dramatic, but enough to obviate a bit the efficacy of the vaccine.

What we are facing now is the potential for a shift where that antigenicity changes so much that we are really naive to this, as Dr. Gerberding just mentioned a moment ago. One of the clear ways of doing that is when a virus jumps species from an animal to a human, and this is what we are seeing with the H5N1 right now in Asia, jumping from chicken to human in Thailand and Vietnam, with the potential of going from human to human.

[Slide shown.]

Dr. FAUCI. This is a chart of the different countries that now have clear-cut bird flu, two of which have transmission to humans, as I mentioned. What is wrong with this picture that is different from years ago is that it is getting worse and worse each year. We usually see a chicken virus that jumps to humans in a very confined location, as we saw last year and a few years ago. We rarely, if ever, see the extent that we see now with nine countries. The reason this is important is that the more chickens that jump to humans, the more humans get infected, and the more humans get infected, the greater the probability of the virus changing enough to develop the capability of going from human to human.

[Slide shown.]

Dr. FAUCI. And when that happens, you have the possibility of a pandemic, as we saw in 1918–1919; whereas, you yourself said, Mr. Waxman, and Dr. Gerberding also, there were tens of millions of deaths for the simple reason that the population of the world was naive to this type of flu. You didn't have the years, if not decades, of memory of similar viruses that you were exposed to.

[Slide shown.]

Dr. FAUCI. So what are we going to do about it? As part of the departmental plan for confronting both pandemic and interpandemic flu, we do the research associated with understanding the pathogenesis and ultimately the basic research that will allow us to develop countermeasures in the form of diagnostics, therapeutics, and vaccines. That is schematically diagramed on this poster here. I want to point out one component of it which is really very important, and that is the revolution over the last decade in genomic research, which allows us not only to very rapidly sequence the microbes to give us a good handle on what we are dealing with, but now an example of what we are calling reverse genetics, where you have the capability of essentially recreating at the genomic level a virus of your choice that clips out the virulence components, but allows the virus to grow very well in whatever media you choose, be it eggs or a cell culture media. And that is what we are doing now with the H5N1 to get a seed virus that could be used for a pilot vaccine.

[Slide shown.]

Dr. FAUCI. And on this last poster, this really summarizes the flowchart of the development of influenza vaccine. It starts off with isolation of the virus in question. The one we are concerned with now, as I mentioned, is the H5N1 that has jumped from chickens to humans. To understand the pathogenesis, to get the proper sequence, to do the molecular manipulation, to get it in a seed form to do a vaccine, and then to make pilot lots and to test those pilot lots in the NIH's network of vaccine trials unit. All of that synergizes with the public health aspects of what the CDC continues to do, as well as other agencies of the Federal Government.

So in summary, the process of preparing for both interpandemic and pandemic flu is complex and is heterogeneous; there is research and there is public health. All of these need to work together to meet these inevitable threats.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Fauci follows:]

Testimony
Before the Committee on Government Reform
United States House of Representatives

NIH's Biomedical Research Response to Influenza and Other Emerging and Re-emerging Infectious Diseases

Statement of
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National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
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Introduction

Mr. Chairman and Members of the Committee, thank you for the opportunity to discuss with you the role of the National Institutes of Health (NIH) in combating influenza and other emerging and re-emerging infectious disease threats. Responding effectively to the challenges posed by diseases such as influenza, SARS, West Nile virus, or HIV requires a multi-faceted, coordinated and focused approach with close collaboration between public health authorities, health care delivery systems, the pharmaceutical industry, and the biomedical research community. The National Institute of Allergy and Infectious Diseases (NIAID), a component of NIH, is the lead Federal agency for conducting, supporting, and coordinating research on influenza and other infectious diseases. As such, NIAID plays a key role in our national effort to prepare for and to respond robustly to the threat of influenza and other emerging infectious diseases.

Emerging and Re-emerging Infectious Diseases

Infectious diseases have afflicted humanity since ancient times, and they will continue to confront us as long as man and microbes co-exist. Unfortunately, the viruses, bacteria, and parasites that cause infectious diseases do not remain static, but continually and dramatically change over time as new pathogens emerge and as familiar ones (such as influenza) re-emerge with new properties or in unfamiliar settings. Such emerging and re-emerging infections have shaped the course of human history while causing incalculable misery and death. For example, importation of smallpox into Central America caused 10-15 million deaths in 1520-1521, effectively ending Aztec civilization. The emerging disease, AIDS, first recognized in 1981, now threatens to surpass in global fatality the plague pandemic of the 14th century and the influenza pandemic of 1918-1919—two other emerging infections that each killed tens of millions of people.

In the past five years alone we have witnessed the introduction of West Nile and monkeypox viruses in the United States, as well as the emergence of a new infectious disease, SARS. In addition, we were confronted in 2001 with a third category of threat, a disease resulting from the deliberate release of an infectious agent, in the form of the anthrax bioterrorist attacks in the United States. Today, we are concerned about sudden outbreaks of diseases such as anthrax, smallpox, and plague not because we expect them to re-emerge naturally, but because they could be released by deliberate human action. Our ability to respond effectively to new infectious disease threats, whether they are emerging, re-emerging, or deliberately introduced, involves many different kinds of activities and many different organizations. From a public health perspective, surveillance and response are the key elements in controlling emerging infections and depend upon rapid detection and containment of pathogens in populations and the environment. Globally, such efforts are coordinated by the World Health Organization (WHO), which recently led the successful effort to contain last year's global SARS outbreak. In the United States, such efforts are led by the Centers for Disease Control and Prevention (CDC), which along with state and local health departments and other agencies recently have made significant strides in national disease surveillance and response capacity. Physicians, nurses, other health care workers and hospitals also must be integrated to respond in a coordinated manner to an outbreak, and the pharmaceutical industry must be fully engaged to develop and manufacture needed diagnostic tools, therapeutics, and vaccines. Within the Department of Health and Human Services (HHS), NIH, CDC, the Food and Drug Administration (FDA), and other agencies all have distinct but complementary roles to play, and have a long history of cooperation. The NIH concentrates on a strong and

focused research program that is critical to preventing and controlling these infectious disease threats.

The conduct, support, and coordination of basic, translational, and applied infectious disease research is the primary responsibility of NIAID. First and foremost, NIAID supports basic and clinical research, which is needed to understand how pathogens cause disease. These research efforts include understanding how microbes replicate, how disease spreads, and what factors lead them to cause serious illness or death. Of particular importance is the understanding of how the body's protective mechanisms, i.e. the immune system, protect against the devastating effects of microbial invaders. In addition, NIAID works closely with academic and industrial partners to translate basic and clinical research findings into new diagnostic tools, therapeutics, and vaccines. This translational and applied research effort also involves close coordination with FDA, CDC, and other Federal agencies to ensure that new countermeasures move as efficiently as possible from the laboratory into general use.

After the anthrax attacks of 2001, Congress dramatically increased funding for biodefense research, much of which was directed to NIH, and to NIAID in particular. NIAID's long institutional experience with infectious disease research of all kinds allowed us to seamlessly take on a greatly expanded biodefense role. Virtually all the fruit of NIAID biodefense activities—including research results, intellectual capital, laboratory resources, and countermeasures in the form of diagnostics, therapeutics, and vaccines—will apply to emerging, re-emerging, and deliberately released microbes alike; recent experience tells us that knowledge developed to understand one pathogen invariably applies to others. For example, when HIV first emerged, antiviral drug development was in its infancy; however, new technologies, many of which were

pioneered at NIAID, have led to the development of more than 20 antiretroviral drugs that can effectively suppress HIV replication and dramatically reduce AIDS morbidity and mortality. These same technologies, and the lessons learned about antiviral drug development, are now being applied to the development of new generations of drugs against many viruses, including influenza, SARS, smallpox, and Ebola.

Influenza Research Activities at NIAID

Influenza can be viewed as a classic example of a re-emerging disease; it is not a new disease, but it continually changes. In most years, influenza viruses that typically infect humans globally undergo small changes in the properties of their surface proteins. If enough of these changes accumulate, the virus is able to escape the human immune response that was primed by prior exposure to influenza viruses or vaccination. This is referred to as "antigenic drift" and it is the basis of well-recognized patterns of influenza disease that occur every year, which nonetheless cause significant mortality and morbidity. In the United States, influenza infections over the past 10 years have resulted in an average of 36,000 deaths and 114,000 hospitalizations each year, and the WHO estimates that the annual average number of deaths worldwide is approximately 500,000. Although only three types of influenza viruses routinely circulate among humans, all known influenza A subtypes are endemic in the gastrointestinal tract of wild ducks. Because the replication machinery of the influenza virus is error prone, as the virus multiplies, avian influenza viruses can emerge that may be able to jump species into domestic poultry, farm animals such as pigs, and humans. This type of significant change in the antigenic makeup of the virus is referred to as "antigenic *shift*". When an influenza virus jumps species from an animal such as a chicken to a human, it usually is a "dead end" infection in that the virus cannot readily transmit further from human to human.

Avian influenza viruses made the jump directly from birds to humans in 1997, but because the virus did not acquire the ability to spread from human to human, only a limited number of deaths (6 out of 18 confirmed cases) occurred. Currently, H5N1 avian influenza viruses in Vietnam and Thailand also have made the jump directly from birds to humans and have resulted in deaths of 18 out of 23 confirmed cases (as of February 9) representing a 78% mortality rate. The fear is that the avian H5N1 and another human influenza virus such as H3N2 might recombine if they were to simultaneously co-infect a person, resulting in the global spread of a new deadly and transmissible human influenza virus referred to as a pandemic strain.

Deadly pandemics are known to have occurred in 1918, 1957, and 1968. The pandemic that occurred in 1918-1919 after an antigenic shift killed 20-40 million people worldwide, including more than half a million in the United States. The pandemics that occurred following other shifts in the virus in 1957 and 1968 killed approximately 2 million and 700,000 people worldwide, respectively. This explains our current high level of concern about the appearance of new forms of virulent H5N1 avian influenza viruses in Asia, which could subsequently recombine with human influenza viruses and result in another pandemic. Given the poor condition of public health systems in many underdeveloped regions and the speed of modern air travel, the consequences of such an event, should it result in an influenza pandemic, would be severe.

The overall goal of the Influenza Program at the NIAID is to support research that leads to more effective approaches to controlling influenza virus infections. This program has two major components, both of which are specified in the nation's draft Pandemic Influenza Preparedness and Response Plan. The first component reflects longstanding programs for interpandemic influenza—research to understand the pathogenesis,

transmissibility, evolution, epidemiology, and the immune response to influenza viruses. These interpandemic research areas include:

- **Basic Research.** NIAID supports many basic research projects aimed at understanding how the influenza virus replicates, interacts with the host, stimulates an immune response and evolves into new strains. Results from these studies lay the foundation for the design of new antiviral drugs, diagnostics, and vaccines.

- **Antiviral Drugs.** NIAID currently supports the identification, development and evaluation of new antivirals against influenza including the screening of new drug candidates to see if they have activity against virus both in laboratory cells and in animals. We also are developing novel broad-spectrum therapeutics intended to work against many influenza virus strains; some of these target viral entry into human cells, while others specifically attack and degrade the viral genome. Development and evaluation of a combination antiviral regimen against potential pandemic influenza strains is also now under way.

- **Diagnostics.** NIAID supports the development of rapid, ultra-sensitive devices to detect influenza virus infection. Although early in development, these devices will allow detection of newly emerging viral mutants and discrimination between different antigenic sub-types.

- **Vaccines.** Because influenza is so easily transmitted, effective vaccines are essential to the control of annual influenza epidemics. The current

egg-based system used to produce licensed influenza vaccines—despite being reliable for more than 40 years—can be improved. Limitations of the current system include: (1) a lengthy manufacturing process; (2) the need to select which virus strains will be in the vaccine at least six months in advance of the influenza season; (3) the need to produce nearly 90 million doses of a new influenza vaccine each year; and (4) the requirement of hundreds of millions of fertilized chicken eggs to manufacture the vaccine. This early decision about which strains to include in the influenza vaccine will not always be correct, and the long lead time required to produce the vaccine makes mid-stream corrective action impossible. Additional limitations could include allergenicity of eggs in some individuals and inability to use eggs for propagation of viruses lethal to chickens.

NIAID is currently supporting several research projects aimed at developing vaccines that can be manufactured more rapidly, are more broadly cross-protective, and are more effective. The use of reverse genetics—a genetic tool developed by NIAID-supported scientists—holds the promise for more rapid generation of high-yielding vaccine candidates that match the anticipated epidemic strain. Reverse genetics also can be used to turn highly pathogenic influenza viruses into vaccine candidates more suitable for vaccine manufacturing by removing or modifying certain virulence genes; laboratories around the world are using the technique to prepare vaccine candidates against the H5N1 viruses emerging in Asia because of the difficulty of using the traditional production methods in eggs. NIAID also is funding the development of new influenza vaccine

technologies. Recently, the NIAID supported a Phase II clinical trial of a new influenza vaccine produced in a cell culture system as an alternative to manufacturing the vaccine in eggs. Another approach has focused on improving the effectiveness of current inactivated vaccines by giving increasing doses of influenza vaccine to elderly individuals, the population which frequently accounts for up to 90% of the influenza deaths each year in the United States. NIAID also is funding the development of new technologies for the production of influenza vaccines. These include DNA-based approaches and broadly protective vaccines based on influenza virus proteins that are shared by multiple strains of the influenza virus. Because NIAID has had remarkable success in the past with ground breaking vaccine research—including advances that led to hepatitis B, *Haemophilus influenzae b*, pneumoccocal pneumonia, and acellular pertussis vaccines, as well as the new live attenuated intranasal influenza vaccine approved by the FDA last year—I am confident that one of the approaches we are pursuing also will lead to a useful, "next-generation" influenza vaccine that can easily be adapted to emerging influenza strains.

- **Surveillance and Epidemiology.** The threat from influenza, like virtually all emerging and re-emerging infectious disease threats, is global in scope. For this reason, NIAID has expanded its activities in other countries in recent years. Through a contract for pandemic influenza preparedness, NIAID supports a long-standing program in Hong Kong to detect the emergence of influenza viruses with pandemic potential in animals. Under this program, Dr. Robert Webster of St. Jude Children's

Research Hospital in Memphis, Tennessee, leads a group that detected the re-emergence of highly pathogenic H5N1 avian strains in this area in 2002 and 2003, and was instrumental in the early detection and characterization of the SARS coronavirus in 2003. This underscores the concept that research on one type of infectious disease often supports or can be applied to research on the other types of infectious diseases, whether newly emerging, re-emerging, or deliberately introduced.

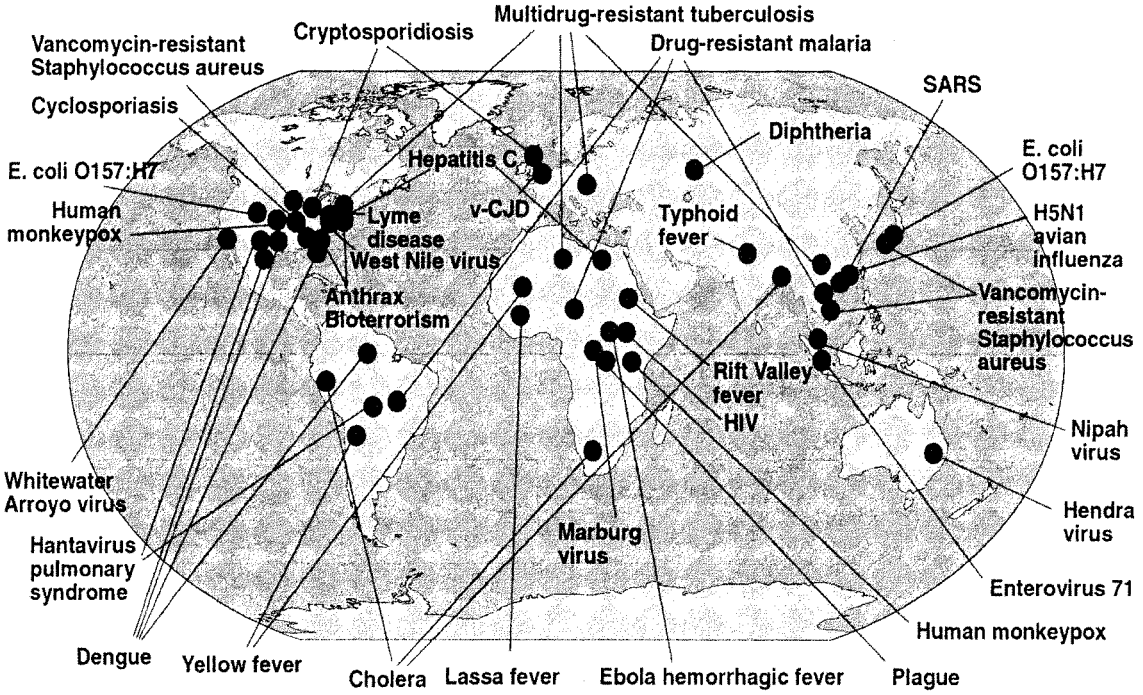
The second component of NIAID's Influenza Program is geared at addressing the emergence of influenza viruses with pandemic potential in humans. After a pandemic influenza strain emerges and a Pandemic Alert has been declared, the draft U.S. Pandemic Influenza Preparedness and Response Plan describes specific roles for NIAID. Foremost among these is to help develop and produce an effective vaccine as rapidly as possible. NIAID would assist in the characterization of the newly emerging influenza strain, create vaccines candidates, develop investigational lots of candidates, and produce and distribute research reagents for use by vaccine researchers in academic and pharmaceutical industry laboratories. NIAID would also work with industry to produce and clinically test candidates at different doses and in different populations in our vaccine clinical trials sites and would coordinate closely with CDC, FDA, and WHO to ensure that a safe and effective vaccine is available to the public as soon as possible. NIAID-supported scientists will also evaluate the susceptibility of the newly emerging virus to the currently available influenza drugs and new drug candidates.

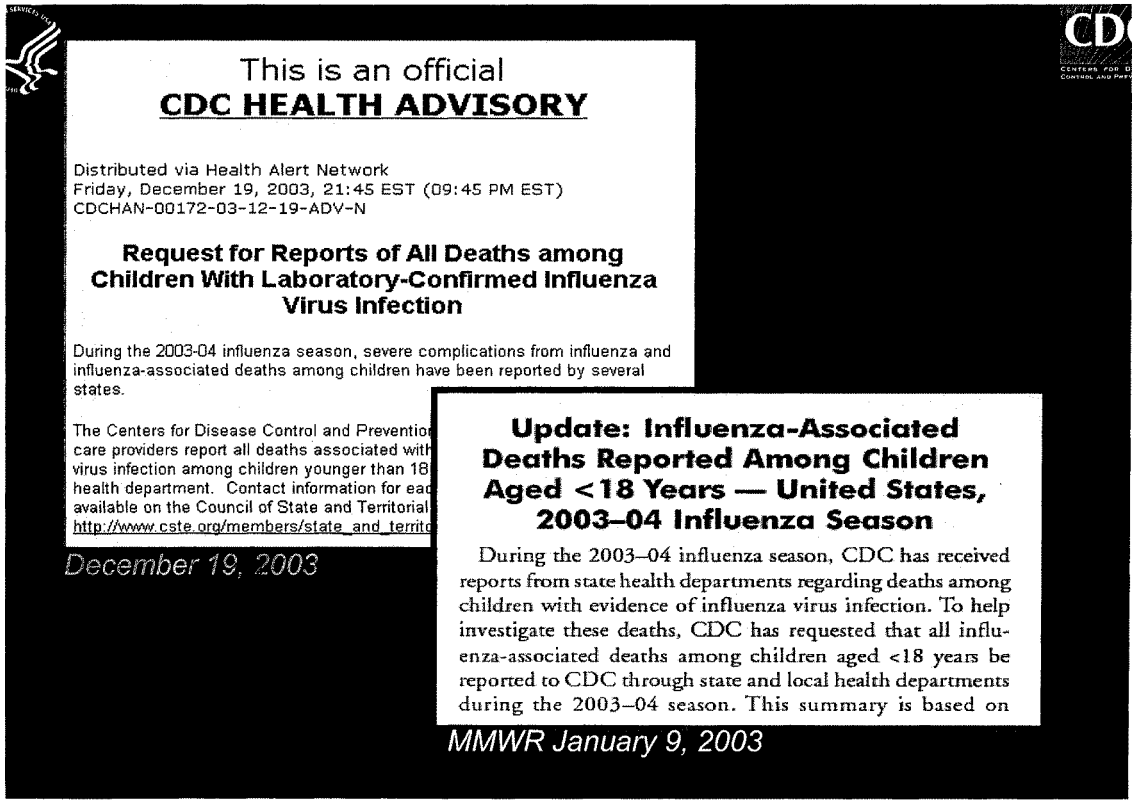
Conclusion

Mr. Chairman, thank you again for allowing me to discuss NIH's efforts to address the threat of influenza. In addition to the significant toll exacted by influenza each year in the United States, the risk of pandemic influenza is significant and the consequences could be very serious. Influenza, however, is one among many ever-changing infectious disease threats confronting our nation and the world that have serious adverse health and economic impact. Fortunately, much of what we learn from the study of one pathogen can often be applied to others. As I have described for you today, NIAID, as the lead Federal agency for infectious disease research, constantly strives to improve our ability to respond to any infectious disease threat, whether emerging, re-emerging, or deliberately introduced by man.

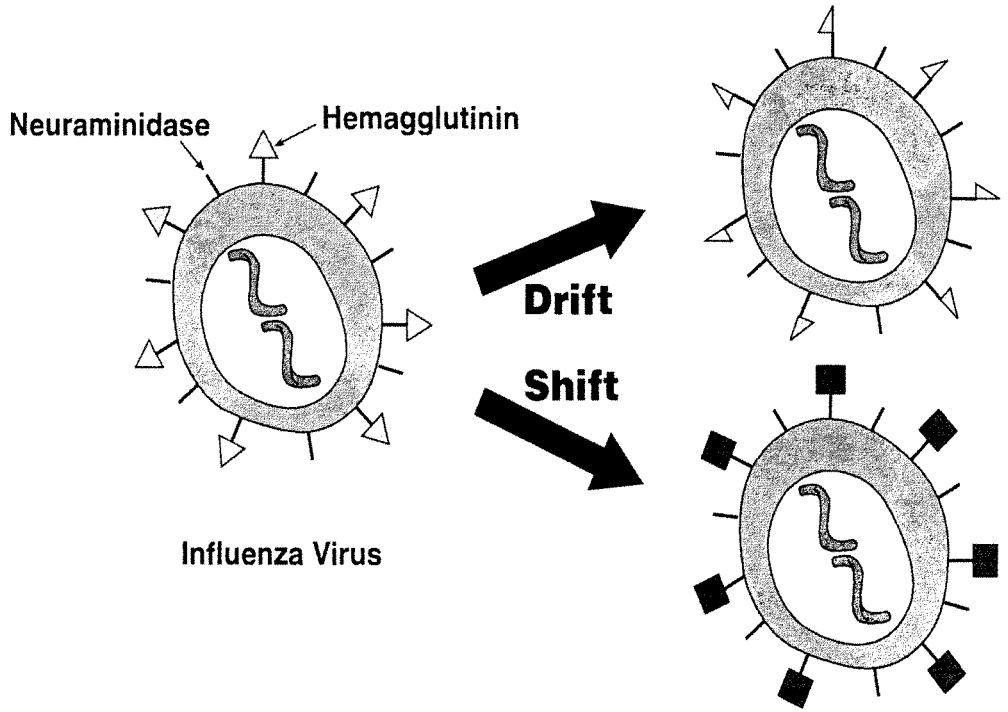
I would be pleased to answer your questions.

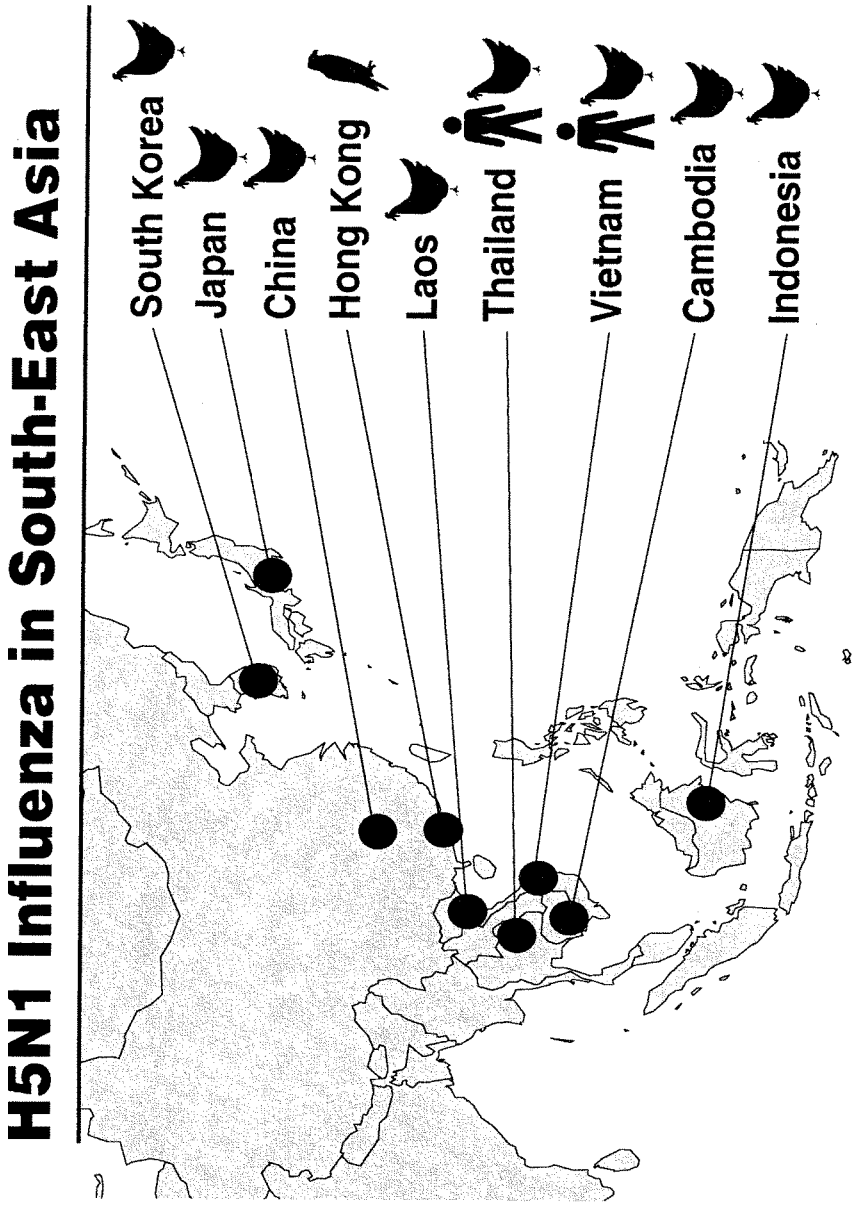
Examples of Emerging and Re-Emerging Diseases



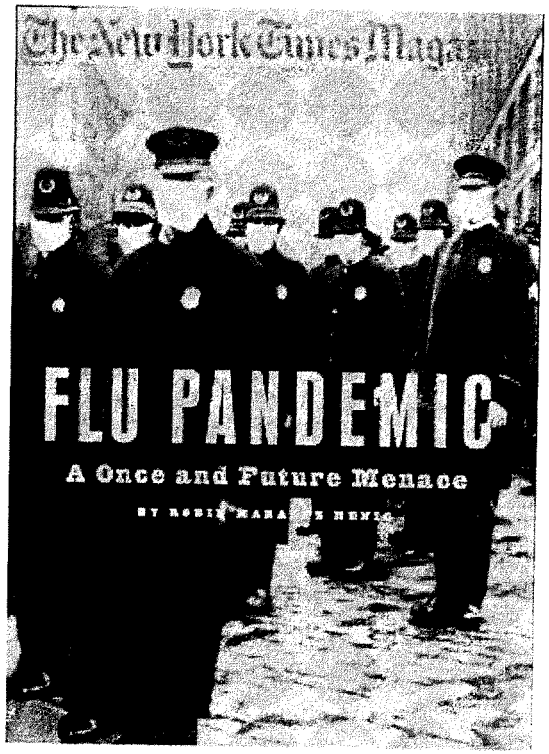

This is an official
CDC HEALTH ADVISORY
Distributed via Health Alert Network
Friday, December 19, 2003, 21:45 EST (09:45 PM EST)
CDCHAN-00172-03-12-19-ADV-N
Request for Reports of All Deaths among Children With Laboratory-Confirmed Influenza Virus Infection
During the 2003-04 influenza season, severe complications from influenza and influenza-associated deaths among children have been reported by several states.
The Centers for Disease Control and Preventio
care providers report all deaths associated with
virus infection among children younger than 18
health department. Contact information for eac
available on the Council of State and Territorial
http://www.cste.org/members/state_and_territo
December 19, 2003
Update: Influenza-Associated Deaths Reported Among Children Aged <18 Years — United States, 2003–04 Influenza Season
During the 2003–04 influenza season, CDC has received reports from state health departments regarding deaths among children with evidence of influenza virus infection. To help investigate these deaths, CDC has requested that all influenza-associated deaths among children aged <18 years be reported to CDC through state and local health departments during the 2003–04 season. This summary is based on
MMWR January 9, 2003

Influenza: Antigenic Drift and Shift

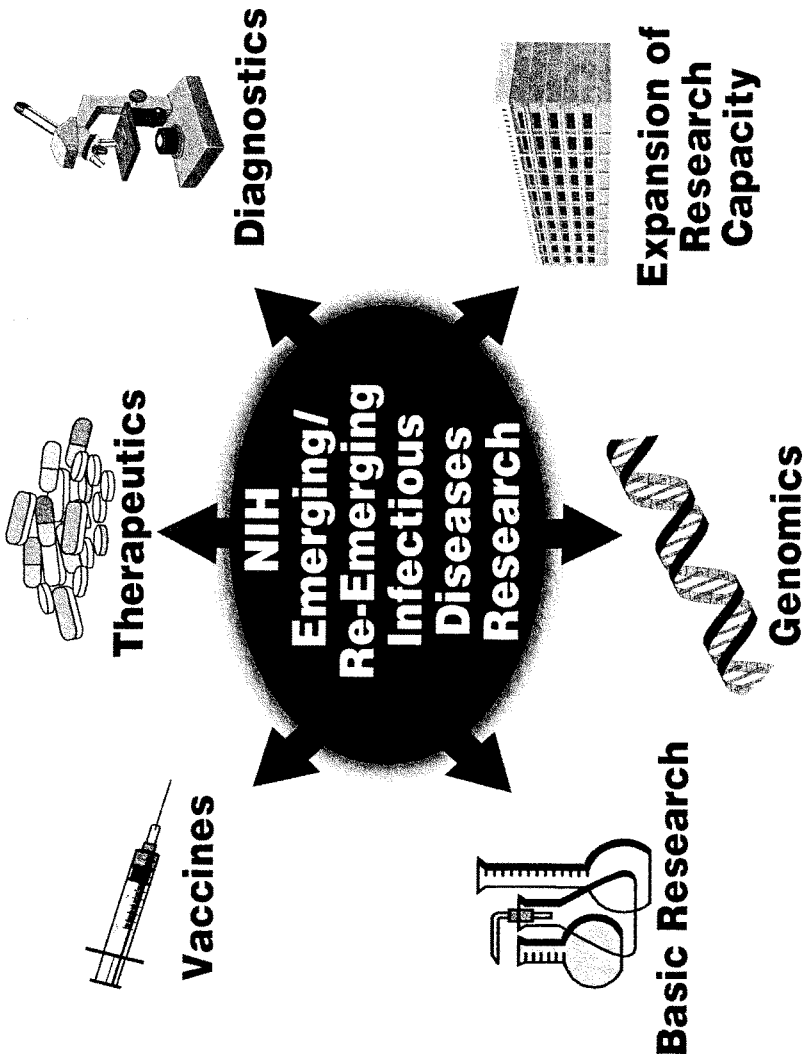



H5N1 Influenza in South-East Asia
South Korea
Japan
China
Hong Kong
Laos
Thailand
Vietnam
Cambodia
Indonesia

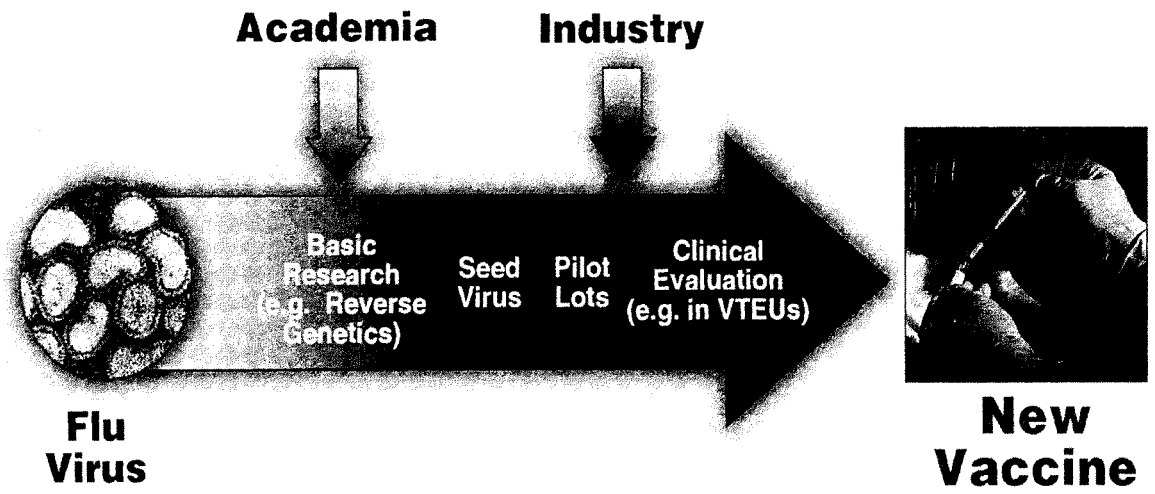
The Influenza Pandemic of 1918-1919



- 500 million people infected worldwide
- 20-40 million deaths worldwide; ~50 percent in people ages 20-40
- >500,000 deaths in United States; 196,000 in October, 1918 alone


NIH
Emerging/
Re-Emerging
Infectious
Diseases
Research
Diagnostics
Expansion of
Research
Capacity
Therapeutics
Genomics
Vaccines
Basic Research

NIH Role in Influenza Vaccine Development



Chairman TOM DAVIS. Thank you very much.

Dr. Heinrich.

Dr. HEINRICH. Mr. Chairman, members of the committee, I too am very pleased to have the opportunity to be here today to discuss our Nation's preparedness for managing public health threats such as these large-scale outbreaks of infectious diseases. Certainly with the SARS outbreak in 2003, this highlighted the challenges in responding to new and emerging infectious diseases, and the recent incidents involving Ricin have raised additional concerns about responding to toxic substances.

To assist the committee in its consideration of our Nation's ability to respond to major public health threats, my remarks will focus on the State and local preparedness, and Federal and State efforts to prepare for an influenza pandemic, and my testimony is largely based on the report that we issued this week.

For the report, we reviewed each State's progress report on the use of approximately $1 billion of bioterrorism preparedness funding that was distributed by CDC and the Health Resources and Services Administration in 2002. The progress reports covered the period through August 2003.

For our report, we also interviewed State and local officials in 10 States and several local jurisdictions. In addition, we updated our prior work on the status of the national and State plans for responding to an influenza pandemic.

We found that as of the summer of 2003, all States had made improvements in their ability to respond to major public health threats, but no aspect of preparedness was fully addressed. In the area of disease surveillance, about half of the States reported having the capacity of receiving and evaluating urgent disease reports on a 24 hour a day, 7 day a week basis. However, only a few States reported having the ability to rapidly detect an outbreak of an influenza-like illness in their State. Similarly, few States reported making efforts to strengthen links between their public health and animal surveillance systems in the veterinary community in order to monitor diseases in animals that may spread to humans, such as the West Nile virus.

All States participate in CDC's laboratory response network, a network of local, State, Federal, and international laboratories that are equipped to respond to emerging threats. However, only about half of the States reported they have the capacity to conduct advanced tests for some of the potential bioterrorist agents.

Most States reported that funding from CDC allowed them to appoint an executive director for their bioterrorism program, designate a full-time person as response coordinator, and hire at least one epidemiologist for each metropolitan area with a population of 500,000 or more. Having dedicated leadership and critical expertise is important; however, the ability to hire and retain personnel is still a major concern for State and local health officials who identify work force shortages as a long-term challenge.

Most States reported that hospitals lack surge capacity to evaluate, diagnose, and treat a large influx of patients with an infectious disease. Furthermore, no State reported having protocols in place for augmenting personnel in response to such an influx of patients. Another concern is that few States have regional plans in place

that would coordinate the response across State borders during a public health emergency.

As we reported previously, Federal officials have drafted, but not finalized, the Federal Influenza Pandemic Plan. In 2000 we recommended that HHS complete this plan, but HHS recently reported that the plan is still under review. States are currently developing their influenza pandemic response plans, but they have had to make assumptions about what the Federal role during a pandemic will be. It is still unclear, for instance, whether the private sector, public sector, or both will have responsibility for purchasing and distributing vaccines and antiviral drugs during a pandemic. These assumptions they are making may prove to be incorrect and cause confusion and disruption of supplies at a critical time if we actually face a pandemic.

In conclusion, while we wish to acknowledge the many positive changes since we last appeared before the committee, and we have documented where States have taken actions to improve their ability to respond to a major public health threat, we see that much remains to be accomplished.

I will be happy to answer any questions.

[The prepared statement of Dr. Heinrich follows:]

United States General Accounting Office

GAO

Testimony
Before the Committee on Government Reform, House of Representatives

For Release on Delivery
Expected at 10:00 a.m. EST
Thursday, February 12, 2004

PUBLIC HEALTH PREPAREDNESS

Response Capacity Improving, but Much Remains to Be Accomplished

Statement of Janet Heinrich
Director, Health Care—Public Health Issues

GAO-04-458T

February 12, 2004

GAO
Accountability · Integrity · Reliability
Highlights

Highlights of GAO-04-458T, a testimony before the Committee on Government Reform, House of Representatives

PUBLIC HEALTH PREPAREDNESS

Response Capacity Improving, but Much Remains to Be Accomplished

Why GAO Did This Study

The anthrax incidents in the fall of 2001 and the severe acute respiratory syndrome (SARS) outbreak in 2002-2003 have raised concerns about the nation's ability to respond to a major public health threat, whether naturally occurring or the result of bioterrorism. The anthrax incidents strained the public health system, including laboratory and workforce capacities, at the state and local levels. The SARS outbreak highlighted the challenges of responding to new and emerging infectious disease. The current influenza season has heightened concerns about the nation's ability to handle a pandemic.

GAO was asked to examine improvements in state and local preparedness for responding to major public health threats and federal and state efforts to prepare for an influenza pandemic.

This testimony is based on GAO's recent report, *HHS Bioterrorism Preparedness Programs: States Reported Progress but Fell Short of Program Goals for 2002*, GAO-04-360R (Feb. 10, 2004). This testimony also updates information contained in GAO's report on federal and state planning for an influenza pandemic, *Influenza Pandemic: Plan Needed for Federal and State Response*, GAO-01-4 (Oct. 27, 2000).

www.gao.gov/cgi-bin/getrpt?GAO-04-458T.

To view the full product, including the scope and methodology, click on the link above. For more information, contact Janet Heinrich at (202) 512-7119.

What GAO Found

Although states have further developed many important aspects of public health preparedness, since April 2003, no state is fully prepared to respond to a major public health threat. States have improved their disease surveillance systems, laboratory capacity, communication capacity, and workforce needed to respond to public health threats, but gaps in each remain. Moreover, regional planning between states is lacking, and many states lack surge capacity—the capacity to evaluate, diagnose, and treat the large numbers of patients that would present during a public health emergency. Although states are developing plans for receiving and distributing medical supplies and material for mass vaccinations from the Strategic National Stockpile in the event of a public health emergency, most of these plans are not yet finalized.

HHS has not published the federal influenza pandemic plan, and most of the state plans have not been finalized. In 2000, GAO recommended that HHS complete the national plan for responding to an influenza pandemic, but according to HHS, the plan is still under review. Absent a federal plan, key questions about the federal role in the purchase, distribution, and administration of vaccines and antiviral drugs during a pandemic remain unanswered. HHS reports that most states continue to develop their state plans despite the lack of a federal plan.

Mr. Chairman and Members of the Committee:

I appreciate the opportunity to be here today to discuss the work we have done pertaining to the nation's preparedness to manage major public health threats. The anthrax incidents in the fall of 2001, the SARS[1] outbreak in 2002-2003, and the recent incidents involving ricin have raised concerns about the nation's ability to respond to a major public health threat, whether naturally occurring or the result of bioterrorism. The anthrax incidents strained the public health system, including surveillance[2] and laboratory capacities as well as the workforce, at the state and local levels.[3] The SARS outbreak highlighted the challenges in responding to new and emerging infectious disease—especially when the ability to identify the disease and a vaccine for preventing it are lacking.[4] The current influenza season has heightened concerns about our nation's ability to handle a pandemic.[5] The Congress has recognized the need to strengthen the nation's ability to respond to such threats and has increased appropriations for federal, state, and local public health preparedness efforts. The Department of Health and Human Services (HHS) has been developing a national plan for responding to an influenza pandemic.

As you requested, to assist the Committee in its consideration of our nation's ability to respond to a major public health threat, whether naturally occurring or the result of bioterrorism, my remarks today will focus on (1) state and local preparedness for responding to major public health threats and (2) federal and state efforts to prepare for an influenza pandemic.

[1]SARS is the abbreviation for severe acute respiratory syndrome.

[2]Public health surveillance uses systems that provide for the ongoing collection, analysis, and dissemination of health-related data to identify, prevent, and control disease.

[3]See U.S. General Accounting Office, *Bioterrorism: Public Health Response to Anthrax Incidents of 2001*, GAO-04-152 (Washington, D.C.: Oct. 15, 2003).

[4]See U.S. General Accounting Office, *SARS Outbreak: Improvements to Public Health Capacity Are Needed for Responding to Bioterrorism and Emerging Infectious Diseases*, GAO-03-769T (Washington, D.C.: May 7, 2003).

[5]Pandemics are worldwide epidemics. Influenza pandemics can have successive "waves" of disease and last for up to 3 years. Three pandemics occurred in the 20th century: the "Spanish flu" of 1918, which killed at least 20 million people worldwide; the "Asian flu" of 1957; and the "Hong Kong flu" of 1968.

My testimony today updates testimony that we provided to you in April 2003[6] and is based largely on work we conducted for our recently released report on HHS's programs that support state and local preparedness for bioterrorism and other public health threats.[7] For that report, we reviewed each state's progress report[8] on the use of bioterrorism preparedness funding distributed in 2002 by HHS's Centers for Disease Control and Prevention (CDC) and Health Resources and Services Administration (HRSA). The progress reports covered the period through August 30, 2003, for CDC's program and through July 1, 2003, for HRSA's program. For that report we also interviewed officials from 10 states, 1 local health department within each of these states, and 2 major metropolitan areas directly funded by CDC and HRSA. My testimony today also updates information provided in our October 2000 report on federal and state planning for an influenza pandemic.[9] To update that information, in February 2004, we spoke with officials from CDC and HHS's National Vaccine Program Office. We conducted our work in accordance with generally accepted government auditing standards.

In summary, although states have further developed many important aspects of public health preparedness, since I testified before you in April 2003, no state is fully prepared to respond to a major public health threat. States have improved their disease surveillance systems, laboratory capacity, communication capacity, and workforce needed to respond to public health threats, but gaps in each remain. Moreover, regional planning between states is lacking, and many states lack surge capacity—the capacity to evaluate, diagnose, and treat the large numbers of patients that would present during a public health emergency. Although states are developing plans for receiving and distributing medical supplies and material for mass vaccinations from the Strategic National Stockpile in the event of a public, most of these plans are not yet finalized.

[6]U.S. General Accounting Office, *Infectious Disease Outbreaks: Bioterrorism Preparedness Efforts Have Improved Public Health Response Capacity, but Gaps Remain*, GAO-03-654T (Washington, D.C.: Apr. 9, 2003).

[7]U.S. General Accounting Office, *HHS Bioterrorism Preparedness Programs: States Reported Progress but Fell Short of Program Goals for 2002*, GAO-04-360R (Washington, D.C.: Feb. 10, 2004).

[8]The progress reports were for the 50 states, the District of Columbia, and the nation's three largest municipalities (New York City, Chicago, and Los Angeles County).

[9]U.S. General Accounting Office, *Influenza Pandemic: Plan Needed for Federal and State Response*, GAO-01-4 (Washington, D.C.: Oct. 27, 2000).

HHS has not published the federal influenza pandemic plan, and most of the state plans for influenza have not been finalized. In 2000, we recommended that HHS complete the national plan for responding to an influenza pandemic, but according to HHS, the plan is still under review. Absent a federal plan, key questions about the federal role in the purchase, distribution, and administration of vaccines and antiviral drugs during a pandemic remain unanswered. HHS reports that most states continue to develop their state plans despite the lack of a federal plan.

Background

The initial response to a public health emergency—for instance an outbreak of an infectious disease—generally occurs at the local and state levels and could involve disease surveillance, laboratory testing, epidemiologic investigation,[10] communication, and health care treatment. As a public health emergency develops, each plays a critical role in an effective response. Local and state health departments collect and monitor data, such as reports from clinicians, for disease trends and evidence of an outbreak. Laboratory personnel test clinical and environmental samples for possible exposures and identification of illnesses. Epidemiologists in the health departments use disease surveillance systems to detect clusters of suspicious symptoms or diseases in order to facilitate early detection of disease and treatment of victims. Public health officials provide needed information to the clinical community, other responders, and the public and implement control measures to prevent additional cases from occurring. Health care providers treat patients and limit the spread of infectious disease. All these response activities require a workforce that is sufficiently skilled and adequate in number.

The federal government provides funding and resources to state and local entities to support preparedness and response efforts. For example, in fiscal year 2002 CDC's Public Health Preparedness and Response for Bioterrorism cooperative agreement[11] program provided approximately $918 million to states to improve bioterrorism preparedness and response as well as other public health emergency preparedness capacities. Similarly, HRSA's Bioterrorism Hospital Preparedness cooperative

[10]Epidemiology is the study of how disease is distributed in populations and the factors that influence or determine this distribution.

[11]A cooperative agreement is used as a mechanism to provide financial support for a particular activity when substantial interaction is expected between the executive agency and a state, local government, or other recipient carrying out the funded activity.

agreement program provided approximately $125 million to states in fiscal year 2002 to enhance the capacity of hospitals and associated health care entities to respond to bioterrorist attacks. HHS renewed these cooperative agreements for the period of August 31, 2003 through August 30, 2004. For these renewed agreements, CDC's program and HRSA's program distributed about $870 million and about $498 million, respectively. Among the other resources that the federal government provides is the Strategic National Stockpile, which contains pharmaceuticals and medical supplies that can be delivered to the site of a public health emergency anywhere in the United States within 12 hours of the decision to deploy them.

The federal government also supports preparedness efforts for an influenza pandemic. HHS's National Vaccine Program Office is responsible for the development of federal plans for vaccine and immunization activities and coordinating these efforts among federal agencies. To foster state and local planning, HHS issued interim planning guidance for the states in 1997 that outlined general federal and state responsibilities during an influenza pandemic. HHS expects that if a pandemic occurs, both the vaccines that are used to prevent influenza and the antiviral drugs that are used to treat influenza will be in short supply.[12] The guidance discussed certain key issues related to limited supplies of the influenza vaccine and antiviral drugs—for instance the amount of vaccine and antiviral drugs that will be purchased at the federal level; the division of responsibility between the public and private sectors for the purchase, distribution, and administration of these supplies during a pandemic; and priorities for vaccinating population groups, such as health workers and public health personnel involved in the pandemic response, and persons traditionally considered to be at increased risk of severe influenza illness and mortality.

[12]These shortages are expected because demand would exceed current rates of production and because manufacturers report that increasing the production capacity of antiviral drugs can take at least 6 to 9 months.

States Have Further Developed Important Aspects of Public Health Preparedness, but Additional Work Is Needed

States reported that as of the summer of 2003 they have made improvements in their preparedness to respond to major public health threats, but no aspect of preparedness has been fully addressed by all of the states.[13] Specifically, although states have strengthened their disease surveillance systems, laboratory capacity, communications, workforce, surge capacity, regional coordination across state borders, and readiness to utilize the Strategic National Stockpile, all of these important aspects of preparedness require additional work.

Disease Surveillance Systems

Although some states have made improvements to their disease surveillance systems, the nation's ability to detect and report a disease outbreak is not uniformly strong across all states. For example, about half of the states reported that their health departments are capable of receiving and evaluating urgent disease reports on a 24-hour-per-day, 7-day-per-week basis; however, few states reported having the ability to rapidly detect an outbreak of an influenza-like illness in the state. Similarly, few states reported efforts to strengthen links between their public health and animal surveillance systems[14] and the veterinary community in order to monitor diseases in animals that may be spread to humans, such as the West Nile virus.[15]

Laboratory Capacity

States have increased their capacity to test and identify specimens and improve laboratory security, although laboratory capacity is not uniformly robust in all states. All states participate in CDC's Laboratory Response Network, a network of local, state, federal, and international laboratories that are equipped to respond to biological and chemical terrorism, emerging infectious diseases and other public health threats. However, only about half of the states reported that they have at least one public health laboratory within the state that has the appropriate instrumentation and appropriately trained staff to conduct certain tests for rapidly

[13]In this section, "state" refers to the 50 states, the District of Columbia, New York City, Chicago and Los Angeles County.

[14]Animal health surveillance involves the collection, evaluation, and interpretation of data to provide timely and accurate detection, diagnosis, prevention, and control of diseases in animals.

[15]For more information, see U.S. General Accounting Office, *West Nile Virus Outbreak: Lessons for Public Health Preparedness*, GAO/HEHS-00-180 (Washington, D.C.: Sept. 11, 2000).

detecting and correctly identifying biological agents. About half of the states reported that they had a facility with a biosafety level sufficient to handle such agents as anthrax.[16] About half the states also reported that laboratory security within the state is consistent with HHS guidelines, which include recommendations for protecting laboratory personnel and preventing the unauthorized removal of dangerous biologic agents from the laboratory.

Communication

Although improving, communication, both among those involved in responding to a major public health threat—such as public health officials, health care providers, and emergency management agencies—and with the public, remains a challenge. CDC's Health Alert Network has been expanded—most of the states reported that the local health departments that cover at least 90 percent of their populations are involved in this network.[17] However, many states reported that they were still in the process of assessing their communication needs. Although about half the states have a plan for educating the public about the risks posed by bioterrorism and other public health threats, few states have mechanisms in place for communicating with the general public during an incident about such issues as when it is necessary to go to the hospital.

Workforce

States have increased the number of personnel essential to public health preparedness, but concerns about workforce shortages remain. Most of the states reported that the bioterrorism preparedness funding from CDC allowed each to appoint an executive director of its bioterrorism preparedness and response program, to designate a response coordinator, and to hire at least one epidemiologist for each metropolitan area with a population greater than 500,000. However, most states continue to have staffing concerns. As we have reported previously,[18] some state and local health officials have had difficulty finding and hiring epidemiologists and

[16]Biosafety measures the degree of protection a laboratory offers to personnel, the environment, and the community.

[17]The Health Alert Network is a nationwide program designed to ensure communication capacity at all state and local health departments. This network enables local health departments to receive health alerts and other information from CDC and state health departments.

[18]U.S. General Accounting Office, *Bioterrorism: Preparedness Varied across State and Local Jurisdictions*, GAO-03-373 (Washington, D.C.: Apr. 7, 2003); GAO-04-360R; GAO-03-654T.

	laboratory personnel. The ability to hire and retain personnel in these areas is still a concern for state and local health officials, who identify workforce shortages as a long-term challenge to their preparedness efforts.
Surge Capacity	Most states lack surge capacity—that is, the capacity to respond to the large influx of patients that could occur during a public health emergency. For example, few states reported that they had the capacity to evaluate, diagnose, and treat 500 or more patients involved in a single incident. Furthermore, no state reported having protocols in place for augmenting personnel in response to large influxes of patients, and few states reported having plans for sharing clinical personnel among hospitals. In addition, few states reported having the capacity to rapidly establish clinics to immunize or provide treatment to large numbers of patients.
Regional Planning	Few states have regional plans in place that would coordinate the response among states during a public health emergency, and state officials remain concerned about a lack of regional planning across state borders. Few states have completed regional response plans for incidents of bioterrorism and other public health threats and emergencies. Most of the states that do have such plans have not established training programs to support their plans or mechanisms to test their plans.
Strategic National Stockpile	Most state plans for using the Strategic National Stockpile in the event of a public health emergency have not been fully developed. All states have prepared preliminary plans for the receipt and management of stockpile materials, but only about a third of the states have plans that outline how they would distribute antibiotics, chemical/nerve agent antidotes, and other materials to areas within the state.

The Federal Influenza Plan Has Not Been Finalized, but State Planning and Other Efforts Continue

Federal officials have not finalized plans for responding to an influenza pandemic, and state influenza pandemic response plans are in various stages of completion.

As we have reported previously,[19] federal officials have drafted but not finalized the federal influenza pandemic plan. In 2000, we recommended that HHS complete the national plan for responding to an influenza pandemic, but HHS reported recently that the plan was still under review within HHS. However, HHS is taking other steps to prepare for an influenza pandemic. For example, CDC has increased the supply of ventilators and added an antiviral drug to the Strategic National Stockpile. HHS is also coordinating with other federal partners, such as the Department of Agriculture, to improve the nation's ability to respond to public health emergencies involving the veterinary and agricultural sectors.

Despite the absence of a finalized, federal response plan for an influenza pandemic, states are developing their own response plans. According to HHS officials, as of February 2004, 15 states have final or draft plans, and 34 states are actively working on plans. In these plans, states have had to make assumptions about what the federal role during an influenza pandemic will be. It is still unclear whether the private sector, the public sector, or both will have responsibility for purchasing and distributing vaccines and antiviral drugs. Some states have assumed that vaccine supply will be under the control of the federal government, while others have assumed that it will not. States have also made different assumptions about who will pay for vaccines, antiviral medications, and related supplies.

Concluding Observations

States have taken many actions to improve their ability to respond to a major public health threat, but no state has reported being fully prepared. Federal plans for the purchase, distribution, and administration of vaccines and drugs in response to an influenza pandemic still have not been finalized, complicating the efforts of states to develop their state plans and heightening concern about our nation's ability to respond effectively to an influenza pandemic. States are more prepared now, but much remains to be accomplished.

[19]GAO-01-4; GAO-03-654T.

Mr. Chairman, this completes my prepared statement. I would be happy to respond to any questions you or other Members of the Committee may have at this time.

Contact and Acknowledgments

For further information about this testimony, please contact Janet Heinrich at (202) 512-7119. Angela Choy, Maria Hewitt, Krister Friday, Nkeruka Okonmah, and Michele Orza also made key contributions to this statement.

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Chairman TOM DAVIS. Thank you very much.

Let me thank all of you. I think it was excellent testimony.

Dr. Gerberding, let me start with you. I noticed the President's budget submission includes, as Mr. Waxman noted, a cut of $105 million for State and local preparedness, but there is a new public health tool called the Bio-Surveillance Initiative. Does that balance off? Can you explain how that works? Are we going to be better prepared or would we be better off restoring the $100 million in addition, or do you have any thoughts on that? Not to put you on the spot.

Dr. GERBERDING. I am used to it.

As we just heard from the GAO, the States still lack the capacity in all jurisdictions to rapidly detect an emerging threat, to alert people 24/7 out to the distal nodes of the response system, and what the President's initiative is designed to do is to accelerate our capacity to detect events at the Federal, State, and local level. So what we are doing with that investment is creating systems that allow us to get real-time data from a variety of sources and to identify the emergence of a health threat and immediately communicate that back. Already we are receiving about 350,000 lab reports a day, we are getting information from nurse call lines around the country, we are receiving clinical data from the DOD and the VA, and we are synthesizing all that information and creating systems to work with the State and local jurisdictions to accomplish this detection and response mode much more quickly. So while there is a reduction in the State-to-State allocation for these activities, we do have this new investment and this new tool that we think will organize and orchestrate this on a much faster timeline than doing it 50 times.

Chairman TOM DAVIS. OK. Let me ask you, and maybe Dr. Fauci as well, how effective are vaccines? If you are vaccinated, does that give you a 99.9 percent immunity? Why do some people get the flu and others don't when they have the same exposure? Just kind of a primer. I was a political science major.

Dr. FAUCI. Well, that is actually an excellent question that frequently gets asked. In a year in which the vaccine matches the circulating strain of flu, in a healthly young person it ranges from 70 to 90 percent effective. As you get into elderly individuals, the capability of the vaccine to protect against the strain in question diminishes considerably, sometimes as low as 50 percent. And when there is a mismatch, even though it was only a slight to modest mismatch, as we saw this year, it sometimes can go down to 30 to 50 percent of efficacy.

It really varies rather considerably on the health status of the individual who is vaccinated, and that is why you see it diminish with age and in people who are immunosuppressed, people who are on immunosuppressive drugs, people with HIV infection, people like that; the capability of their immune system to appropriately respond to a vaccine gets less and less. But in an otherwise healthy, young individual it ranges between 70 and 90 percent.

Chairman TOM DAVIS. And I guess even if you don't have the vaccine, some people get exposed and don't have many symptoms.

Dr. FAUCI. Oh, without a doubt.

Chairman TOM DAVIS. Because their immune systems are just strong.

Dr. FAUCI. Yes. And there is a range of responses to a wild type or confrontation with a circulating virus, such that somebody might get infected and have such a subclinical illness that they don't even know they are infected. And there is a whole range of people who have mild illness, moderate illness, and then there is a very small percentage of people who do very, very poorly; they get very sick and sometimes life-threateningly so, and that is usually less than 1 percent.

Chairman TOM DAVIS. But you can walk around vaccinated, and there are still other flu strains out there that can nail you.

Dr. FAUCI. Oh, absolutely. There is no question about that, yes.

Dr. GERBERDING. If I could just add one thing, though.

Chairman TOM DAVIS. Sure. Please.

Dr. GERBERDING. Because the vaccine really does save lives. So we don't want to give people the impression that there is no advantage to vaccination. It is clearly a life-saving intervention.

Chairman TOM DAVIS. There are other members who brought this up, that vaccinations can cause the flu itself, where you get people reacting that get it and otherwise wouldn't because their systems respond.

Dr. GERBERDING. This is a common misunderstanding, because sometimes the flu vaccine itself causes an inflammation or a small reaction. But flu vaccine absolutely does not give you flu if you are using the inactivated vaccine, because all the virus particles are dead. The new flu vaccine that came out this year, that you put in your nose, is an attenuated strain of virus; it is still alive, and so it causes a very mild infection that is limited to your nasal tissues. That vaccine sometimes is associated with fever and some very minor cold-like symptoms. But none of the virus vaccines actually cause flu.

Chairman TOM DAVIS. So there is agreement on that.

Dr. FAUCI. There is no question about it. In fact, you often hear we, as physicians, sometimes hear, I know Dr. Gerberding and I both have people say, "No, I got the flu shot and the next day I got the flu, so the flu shot must have given me the flu." It is physically impossible for that to happen with a killed virus.

Chairman TOM DAVIS. And on the nasal side, there was something on a Web site this year. Was it misleading? I know there has been some talk that it can cause flu.

Dr. GERBERDING. As I said, the virus in the vaccine, the nasal vaccine, is a very weak virus, and it is temperature sensitive, so it doesn't grow well at normal temperatures. And it does not actually cause disease, but the hypothetical concern is that if you passed even this weak virus on to someone with a very depressed immune system, as Dr. Fauci was saying, that it could theoretically cause infection in that individual. So as a precaution we recommend that people who receive this very effective FluMist vaccine don't have direct contact with others who are very immunosuppressed.

Chairman TOM DAVIS. OK, thank you. I may followup on that, but it is Mr. Waxman's turn.

Mr. WAXMAN. Thank you, Mr. Chairman.

Dr. Gerberding, all of us in the Congress appreciate your hard work and the hard work and dedication of the scientists at CDC. They are dedicated people, and we commend them for the job they are doing. I said in my opening statement that I am concerned that the President's budget does not provide adequate support for public health. You testified that the new recommendation to vaccinate children between the ages of 6 and 23 months against flu is an important step in saving lives, yet the Virginia State health commissioner is going to testify that the President's budget does not provide adequate funding to assure States will include the flu vaccine in their childhood immunization programs.

Are you concerned that the President's budget does not provide enough funding for the Federal Vaccines for Children program and for the State grants for vaccination efforts to assure that children have access to all recommended vaccines, including the flu vaccine?

Dr. GERBERDING. There has been a change in the way the allocation for vaccines is proposed in the President's 2005 budget. One of the changes is to provide an additional $40 million to stockpile influenza vaccines for children so that we have an additional supply. And in the Vaccines for Children line, these pediatric doses would then be available to amplify the amount of vaccine that we have had in the past. In addition, that change in allocation ensures that additional children will be eligible for childhood immunizations who currently don't qualify under the voluntary program. By putting more money in the mandatory vaccination program, we actually will end up with a net increase in the number of children who can receive vaccines and, in addition, negotiated a much better price for the diphtheria tetanus vaccine that was too expensive for many children to receive in the past.

Mr. WAXMAN. That $40 million flu vaccine stockpile is a reserve supply, it doesn't really address the issue of routine vaccination programs. We are going to hear from others, especially the States, who are going to tell us they feel they are being short-changed. Are you concerned they might have a point?

Dr. GERBERDING. I am always concerned if the States have a perspective. One of the things that we are doing in the department right now is looking at how we can predict what the utilization will be. We are also going back to the ACIP, the immunization advisory board, and evaluating this year's flu situation in children to make sure that our recommendations for limiting the vaccine to that age group still apply, given the concerns about an additional burden of illness in children. So we have to look upon this as a work in progress, and if there are unmet needs, we will do our best to identify them.

Mr. WAXMAN. The GAO is going to report that not a single State has a plan for hospitals to handle an epidemic of at least 500 patients. We are also going to hear from the Trust for America's Health that most States and HHS have not finalized their flu plans, and that only two States have the capacity to receive and distribute emergency medications.

When will State and HHS pandemic flu plans be finalized, and how can we close critical public health gaps as quickly as possible?

Dr. GERBERDING. Thank you. As you know, a plan is one aspect of preparedness, and the formalized big, thick flu plan is not yet

finalized in the department, although I think we do have the final document together. But there is much more important work besides a written plan, and we saw with SARS how rapidly we were able to scale up and develop plans for containing SARS, and actually, as you will see on the CDC Web site, the steps that need to be taken at the local level for managing SARS are the same steps that we would recommend for flu.

Mr. WAXMAN. Well, we are going to hear testimony that additional funding is going to be critical for this to all happen, and the President's budget cuts over $100 million from State and local public health preparedness grants. And in his written testimony today, the Virginia State health commissioner states these cuts could jeopardize our ability to respond to a terrorist event, outbreak of an infectious disease, or other public health threat or emergency.

So it seems to me the States are telling us, even though you answered Mr. Davis' question by saying that there is money because of the biosurveillance program, they are saying they see this all as a cut. If there is a biosurveillance program, that could increase demand for their funds because there can be some sensor that will pick up something, they will have to divert resources to deal with it, and yet we are faced with these public health emergencies as well.

So do you see that the States vigorously disputing this point, that the States are wrong?

Dr. GERBERDING. As you know, we put about $3 billion into the States through the various preparedness activities, and we are constantly looking at the evolution of preparedness building from a pretty dilapidated public health system, and so we have to be able to sustain these investments for the long term to catch up with where we should have been all along.

Having said that, I think that our goal is to achieve a level of preparedness that would be adequate to protect against terrorism as well as emerging health threats, and we have seen some very encouraging examples this year where the investments really have paid off, with the meningitis outbreak in Chicago, the hepatitis A outbreak in Pennsylvania.

Mr. WAXMAN. Well, I am sure the investments are improving, but if we are not making the full investment we need, we are not going to get to the point where we must be if we are going to face a crisis.

I do want to ask one question of Dr. Fauci before we move on. Experts have said that a bird flu vaccine is urgently needed. What is the progress on such a vaccine? Should vaccine companies be producing bird flu vaccine right now?

Dr. FAUCI. The process of developing a vaccine for bird flu that might infect humans has already been launched, namely, the seed viruses are now in hand to a number of groups, including the CDC and the NIH. They are being produced and we are negotiating now for the development of pilot lots that will be used in phase 1 studies to determine not only the safety, but what the dosage would be. That whole process of getting a seed usually takes from weeks to a month, of getting a pilot lot usually takes a couple of months, and then an additional 6 months to have the vaccine available. So we are already going in that direction.

We must caution that it is a work in progress, because if there is a virus that goes from chicken to human, which is what we are all concerned about, and if it then assumes the capability of going from human to human, it might change such that it is a bit different from the original virus that went from the chicken to the human. So you have to move ahead, because you can't wait, but you have to keep your eye on what is evolving out there in the field.

Mr. WAXMAN. Thank you.

Thank you, Mr. Chairman.

Chairman TOM DAVIS. Thank you very much.

The gentleman from Tennessee.

Mr. DUNCAN. Thank you, Mr. Chairman.

I understand from some of the briefing materials that about 87 million people, or about 30 percent of our population, got vaccinated this past flu season. Is that roughly correct?

Dr. GERBERDING. We don't have the final information yet, but our best estimate is about 87 million, and that is the largest number of people we probably have ever vaccinated.

Mr. DUNCAN. And then we are also told that ordinarily 10 to 20 percent of Americans get contagious respiratory illness annually. We have said 30 percent got vaccinated, but of the total population, of the 285 million people we have in this country, how many people contracted this flu this season?

Dr. GERBERDING. It is too early for us to give you the absolute answer to that, but in general, on an average year it is between 10 and 20 percent of all people get influenza; obviously, most of them very mild disease.

Mr. DUNCAN. And I am not sure exactly how this works. I understand there were three companies that came up with the vaccine this season?

Dr. GERBERDING. In the United States there are three vaccine manufacturers that contributed to our supply. There are other manufacturers around the globe, including companies that make vaccine for the Southern Hemisphere, which usually has a little bit of a different influenza profile than the Northern Hemisphere; and the timing in the Southern Hemisphere is out of sequence with ours.

Mr. DUNCAN. And how is this paid for? Because I have seen programs where they give out free flu shots and then other places where they charge. Are these companies totally compensated by the Federal Government or is it part Federal and part private, or how is it done?

Dr. GERBERDING. For influenza immunization, the vast majority of the program is in the private sector, so it is administered through health plans and private clinician offices and so forth. A small proportion is in the public sector. For those of us in public health, that is the part of the vaccination program that is the easiest for us to monitor and to keep track of, but we are developing new systems so that we will be able to have a much bigger picture of the whole vaccine supply; where it is, how it is being distributed, who has it and who doesn't.

Mr. DUNCAN. And you just said that you sent $3 billion to the States?

Dr. GERBERDING. Over the last 3 years the terrorism preparedness funds. That is an approximate figure based on what CDC puts out and what HRSA puts out to the hospital preparedness component.

Mr. DUNCAN. But you said that wasn't just for vaccines, that was for education and all kinds of things.

Dr. GERBERDING. That money is for six things: for surveillance, for planning, for laboratory capacity, for information technology, for communication, and training.

Mr. DUNCAN. Well, rough guess, what percentage of that $3 billion would have been spent on the vaccines themselves?

Dr. GERBERDING. Very little of that money would be spent on purchase of vaccines, because that is not what the money is specifically for.

Mr. DUNCAN. And the gentleman doctor, I am not sure how you pronounce your last name.

Dr. FAUCI. Fauci.

Mr. DUNCAN. Fauci? You said that these vaccines were 70 or 80 percent effective in younger people and in older people it was 50 percent or maybe even less?

Dr. FAUCI. That is correct, yes. It varies. The older anyone gets, even if they are a relatively healthy older person, as you get older, beyond 60 or so, your immune system does not respond as robustly as the immune system of a 20 or 30-year-old. So the efficacy diminishes proportionately, although it varies. There may be older people who have a very good response and are really quite well protected.

Mr. DUNCAN. And I read that each year the health authorities try to pick three strains of the virus?

Dr. FAUCI. Yes.

Mr. DUNCAN. In advance?

Dr. FAUCI. Yes. What happens is that, as Dr. Gerberding mentioned, toward the end of the winter, the CDC, WHO, and FDA get involved in doing a surveillance of the strains that are out there, and in the influenza vaccine shot that you and I get, it contains two As and a B. For example, this year had an H3N2, which was the Panama strain; it had an H1N1; and it had an influenza B.

Mr. DUNCAN. Well, let me ask you this, since my time is so short. How many strains are there out there that you choose from to get these three?

Dr. GERBERDING. Overall, there are 15 main types of H1s, three of which are in humans. But the subtypes of those are infinite. So each little point mutation in the virus can create a new strain, and we just can't predict.

Mr. DUNCAN. Because that is what I had heard somebody say at another time, that there were so many possibilities, it is almost unbelievable.

Dr. GERBERDING. That is absolutely right.

Mr. DUNCAN. And it says the effectiveness of the vaccine is dependent on whether the strains picked will be the same strains to circulate during the following flu season.

Dr. FAUCI. There will always be minor strains, but what we try to do is to make the best guesstimate of what the predominant strain that will circulate the following season is. And generally we are right about 9 out of 10 times, 8 or 9 out of 10 times.

Mr. DUNCAN. Well, I have some more questions, but my time has run out.

Chairman TOM DAVIS. We may do another round, but thank you very much.

Gentleman from Maryland, Mr. Van Hollen.

Mr. VAN HOLLEN. Thank you, Mr. Chairman.

Thank all of you for your testimony.

Dr. Gerberding, I just want to take this opportunity to followup on a hearing we had in this committee last October regarding the future of the Commissioned Corps of the Public Health Service and the reorganization plan. And I know you weren't here at that hearing, but at the time we had a survey from some of the commissioned officers at the CDC which made it clear that they were not happy with the direction that the reorganization was taking and, in response to questions, many of them said that if it was implemented as proposed by HHS, that they would seriously consider leaving the CDC, because it had a number of requirements that seemed to be not appropriate for some of the scientists at CDC, for example, emergency deployments in areas outside their area of expertise, certain physical fitness requirements which might not have really been applicable. And, in fact, Dr. Carmona, the Surgeon General, said sending officers such as epidemiologists from CDC to achieve mission objectives that are not consistent with their specific training and physical capabilities makes no sense.

My understanding is, however, HHS has gone ahead and implemented the reorganization plan without the changes the Surgeon General said he wanted to make in that plan, in his testimony before this committee last October. So my question to you is, is that in fact the case and what impact is it having on the Commissioned Corps officers of the CDC? Have you gotten any feedback from them? And what actions, if any, do you intend to take?

Dr. GERBERDING. I was very concerned about the results of the survey that you described. We met with Secretary Thompson immediately thereafter, and he was very adamant that his intention is to improve the corps and to strengthen the corps and expand the corps, and in no way does he want to interfere with the capacity of the CDC Commissioned Corps officers to function as effective disease detectives. So since that time we have set up a series of interventions, better ways to communicate what the Commissioned Corps needs are, and we have proposed to the department a special track in the Commissioned Corps for public health officers that is under review right now that would accommodate the needs of the Commissioned Corps and still allow the Secretary to fulfill his mission of having a much stronger and a much more robust Commissioned Corps. So we would be happy to talk with you about those proposals, and just to say that there is a lot of dialog going on right now to try to make this go in the best possible way to achieve the mission.

Mr. VAN HOLLEN. OK, so HHS hasn't made any final decisions with respect to the provisions I referred to.

Dr. GERBERDING. The last communication we had was the next round of the draft proposals, and to my knowledge there has been no formal decision about the overall transformation.

Chairman TOM DAVIS. If I might intervene. Not to take your time, but Mr. Waxman and I both sent a letter to HHS expressing our concerns, and we are waiting for a reply as well.

Mr. VAN HOLLEN. I believe you sent a January letter, and I just want to make sure that the committee's concerns are being heard, and I understand your concerns as well. I just want to make sure they are being heard, and if you can keep us informed about it.

Dr. GERBERDING. Thank you.

Mr. VAN HOLLEN. Because it seemed to have a potentially very large impact on CDC based on that survey.

Dr. GERBERDING. Thank you. I will make sure that the Secretary hears your comments today. But I will just tell you right now that I am absolutely confident that he wants this to work, and he wants this to work right, so his door is open to us and we are going to work this out.

Mr. VAN HOLLEN. Thank you.

And, Dr. Fauci, it is wonderful to have you at NIH and my congressional district, so welcome again.

Chairman TOM DAVIS. OK. Let me go with a few other questions.

Dr. Heinrich, the best initial defense against public health threats continues to be, from what I judge from everybody's testimony, accurate, timely recognition and reporting of problems. People out there in the field, when something happens, are letting us know about it. How well developed are information sharing networks between States and the Federal Government at this point, and do these networks protect privacy while seamlessly connecting government at all levels?

Dr. HEINRICH. Actually, in the area of the communication electronic network, that is one of the areas where I think there has been the most progress from our reviews. We have heard from some of the State officials that information seems to flow best from the Federal level down, as opposed to the local county through the State up, but those information systems do seem to be working.

Chairman TOM DAVIS. OK.

Let me ask Dr. Gerberding, how effectively did CDC coordinate work with the State and local public health officials to respond to this year's flu season? Were these efforts reflective of how you and State and local officials respond to a greater public health threat?

Dr. GERBERDING. Thank you. On December 5th I activated the CDC's emergency operation center to coordinate our response to influenza because we recognized with this fast propagation of the outbreak we needed to have the best possible logistic support. So we implemented our emergency communication system, we provided regular updates, we had routine conference calls with State and local health officers. We did our very best to provide the ongoing information and then worked with the bi-directional communications system to try to track vaccine shortages and redistribute vaccine as indicated. We also fielded information about the need for pediatric vaccine and anti-retroviral drugs. Secretary Thompson was able to authorize some emergency purchases of both vaccine as well as anti-retroviral drugs for the stockpile, and I think overall we built on our experience with SARS, monkeypox, and West Nile virus and continued to scale up and speed up our integration at those levels.

Chairman TOM DAVIS. OK.

Dr. Fauci, the purpose of Project Bioshield is to stimulate companies to develop modern and effective vaccines, drugs, and devices to protect Americans in the event of a bioterrorist attack or a public health emergency. Do you think we need similar incentives to increase production capacities for flu vaccine manufacturers?

Dr. FAUCI. I think we need to appreciate and recognize that, in general, transcending biodefense, we have a very tenuous situation vis-a-vis vaccine development because there are too few companies involved, and the incentives for companies to make the risky investment in the development of a vaccine are such that we really are walking on thin ice when it comes to vaccines in general; and that would apply even to influenza. In general, I think Bioshield was a very important step in trying to shore that up and prevent any potential serious problems in going forward with vaccines and other countermeasures in biodefense.

That doesn't alleviate the problems that we have in general, and what we have been having to do is work more closely with the companies to push even further in advance development to take away some of the risk that they take, because if you look at the incentive of developing a product in which the risk benefit vis-a-vis profit is considerably less than a drug, for example, that is very widely used, the numbers speak for themselves. I mean, there is the classic story that the amount of money made on a single lipid-lowering drug essentially eclipses all of the vaccines put together. So we really do have a problem with vaccine development in that regard.

Chairman TOM DAVIS. Is there a flu season where it tends to peak and we talk about a flu season getting ready, and why is it a certain time? I mean, it is with us all the time, the virus is present at all times. Is there a particular season, and why is that?

Dr. FAUCI. Well, in our hemisphere, the season generally goes in the winter.

Chairman TOM DAVIS. Are you on? See if your mic is on.

Dr. FAUCI. Oh, I am sorry. The season in our hemisphere, in the United States, Canada, etc., generally starts in the early winter, December, and generally peaks in January, and then tapers off as you get to February, and usually is gone by March. That is not necessarily the case in other regions where the temperature is essentially constant or practically constant throughout the year. That is the point that Dr. Gerberding made just a few minutes ago. With this year, the cases that we were seeing were unusually early, which triggered the response of people wanting to get vaccinated.

Chairman TOM DAVIS. Why is it at that time? I mean, is it the cold weather that brings it on?

Dr. FAUCI. It is a combination of things. The most obvious that we say, and yet there is some scientific softness about this, but the generally appreciated explanation is that in the winter months you have people crowded together and indoors without a lot of good ventilation, so that when you have a respiratory-born virus, be it influenza or several others, the possibility of their transmitting from person to person by aerosolization or droplets increases as more people spend more time in situations indoors. That is one of the possibilities.

There are also some studies showing temperature and moisture and other considerations that allow a respiratory-born pathogen to be able to be transmitted better or not, depending upon the humidity and depending upon the temperature.

Dr. GERBERDING. I would just add one perspective. In this world of globalization and connectivity and speed, while we have a flu season here in the winter months, it is flu season in the summer months in the Southern Hemisphere. So if you looked at the globe, at any given time of the year there is flu virus circulating, and that is something that we have to come to grips with as we see now how these viruses can move so quickly throughout the world.

Chairman TOM DAVIS. That is what prompted the question. Why here do we seem to have a peak season, although I guess people get it all the time? And we try to see when a strain is developing, why information is so important is we see something new developing somewhere; we want to stay ahead of it before it becomes a much more massive problem.

Mr. Waxman, you had some additional questions.

Mr. WAXMAN. Dr. Gerberding, CDC and the Health Resources Service Administration developed critical benchmarks to measure progress by the States. This is a very important process, but for it to work the benchmarks have to be meaningful. In hospital preparedness, one of the critical benchmarks is that each State must be able to provide initial evaluation and treatment to 10 adult and pediatric patients at a time in the entire State. Certainly this is not a meaningful standard for California, and maybe not for any State.

I am concerned that some of these standards have been set to correspond to what is achievable under current levels of funding, not what is needed for true public health preparedness. This puts the cart before the horse. Is CDC or HRSA under any pressure to alter critical benchmarks to match the funding?

Dr. GERBERDING. Actually, what we are doing right now is moving beyond the kinds of generic benchmarks that were included in the original guidelines, and we are moving to performance-based benchmarking, where we actually define the capacities. And specifically with respect to flu, in the 2003 budget allocation we have much more targeted benchmarks that deal specifically with influenza. But what we would like to do at this point in time, now that we have had a chance to build some basic infrastructure capabilities, is to really hone in on what exactly does it mean to be prepared and how will we realistically know that. We are working with the State and local health departments to define those new benchmarks.

Mr. WAXMAN. Well, Dr. Heinrich, maybe you can comment on this. Have they thrown out these old benchmarks? Are they no longer meaningful and, therefore, they are meeting certain performance standards that match the needs for public health?

Dr. HEINRICH. In our review and in our discussions with State and local officials, overall, people found the benchmarks quite helpful in giving them guidance as to how to set priorities, and, of course, each area varies considerably State by State, and even within State. We did hear many times that when there were specific numbers attached to benchmarks, it was not always meaning-

ful. For example, what you just said, for a State to say that they could manage an influx of 500 people in a State as large as California.

Mr. WAXMAN. Well, it is even less than that. Each State must be able to provide initial evaluation and treatment to 10 adult and pediatric patients to respiratory isolation rooms in the entire State. Now, my question is, is this a benchmark that is meaningful health or is it, one, being driven by the pressure for CDC or HRSA to match the funding and to set the target so low, the benchmark so low that it is based on the funding amounts?

Dr. HEINRICH. And I don't know what the rationale is for those particular numbers. When we asked officials at the Federal level and others, we didn't really get any good answers.

Mr. WAXMAN. Well, let us see if maybe Dr. Gerberding can give us a good answer.

Dr. GERBERDING. The benchmark you are referring to is part of the HRSA grant, and so I am not prepared to explain it to you in detail, but I would be happy to make sure that you get the explanation that you are asking for.

Mr. WAXMAN. In your professional judgment, is that a reasonable benchmark for HRSA?

Dr. GERBERDING. In my professional judgment, the benchmark should be based on what is necessary to get the preparedness level accomplished that we have set out to accomplish. We are staging preparedness, because you can scale up to any level of threat imaginable, and it is not realistic to expect people to be prepared for the worst case scenario the first time out, but we are moving up the scale every single time we put money out.

Mr. WAXMAN. We can also scale down to something that sounds absurd simply because the money might not be there. So that is a concern I raise.

There are concerns that the bird flu that is affecting both chickens and people in Asia could be a flu pandemic and my question for you, Dr. Gerberding, is how many doses of vaccine for bird flu or another pandemic strain could FDA license manufacturers produce quickly in case of a flu pandemic? And is this capacity sufficient to meet the public health needs of the United States?

Dr. GERBERDING. Well, that is a complicated question. I will try to give you a short answer. With the preparation of a bird flu vaccine, where we are starting a new manufacturing process with a new product, we are already using reverse genetics for this and in an emergency would probably be able to use a tissue-based culture system and only make a single, as opposed to a trivalent, product. Our manufacturers right now, based on their current production, could make 270 million doses of a monovalent vaccine in the same amount of time that we make the trivalent vaccine.

So 270 million doses is pretty close to the U.S. population, and that would be an optimistic projection. That all assumes that timing goes well and that we have the egg capacity and the other things that we would need to be able to do this, or that we can quickly get a safe licensable tissue culture system.

Mr. WAXMAN. One of the three FDA licensed vaccine manufacturers produces vaccine for the U.S. market in the United Kingdom, and this company will testify that in the event of a pandemic, the

United Kingdom may prevent them from exporting vaccine to the United States. In the case of a flu pandemic, how can we be sure that this company will be allowed to export vaccine to the United States? And if not, what impact would that have on the flu vaccine supply? And what has HHS done to encourage vaccine manufacturers to produce vaccine in the United States?

Dr. GERBERDING. Well, that is another area of importance. We recognize that over the years there have been fewer and fewer manufacturers engaged in vaccine production, and that creates vulnerabilities. Some years it creates a vulnerability in terms of the timing of the availability of the vaccine; other years, like this year, there was a problem with the total amount of vaccine produced. I think, as I mentioned, the Secretary has told us that we need to include steps now to expand the production capability of vaccine in the immediate sense, but also in the longer-term sense, to really look at what needs to happen to incentivize manufacturers to be in this business. And we are assembling, through the National Vaccine Advisory Committee, this spring a summary, comprehensive, top-to-bottom review of what needs to be done about this problem at the Secretary's request. So we will be able to come back to you with some specifics on that very soon.

Mr. WAXMAN. Have you looked at the possibility that we might be barred from exporting from that factory in Great Britain?

Dr. GERBERDING. That is a vulnerability that we are aware of. We have similar problems with antibiotics at times, and so that is one of the things that has to be addressed in this review.

Mr. WAXMAN. And just one last question for Dr. Fauci. We are looking at a prospect for a vaccine that would be cell-based as opposed to egg-based, and it could be then produced in a shorter time. What is your view of the future of cell-based vaccine? And if the cell-based vaccine is the wave of the future, are you concerned that vaccine manufacturers are going to be less willing to get into the egg-based flu vaccine market, since the sense is that the technology may become obsolete? Would this create a problem during the transition?

Dr. FAUCI. I believe that it is essential to pursue alternative methods of producing vaccines. The egg-based method has been tried and true, and has served us very well. There are some potential difficulties with that, particularly in a situation in which a virus may not grow well in the egg or might actually destroy the egg, particularly if it has virulence factors for eggs being a bird flu. We can get around that partially, or attempt to, by reverse genetics, which essentially clips out those virulence factors that would be detrimental to the eggs.

But notwithstanding that, we need to do both in parallel, and that is exactly what we are doing. We are doing research right now with several of our grantees to try and develop a cell-based tissue culture approach toward the development of vaccines. Some of the drug companies are even doing it on their own.

What I detect in my discussions with the pharmaceutical corporations is that they are aware that we need to do those in parallel, and I hope, but I think there will be an easy transition so that we will have both going and we will be able to go to one or the other, depending upon the situation.

Mr. WAXMAN. Thank you, Mr. Chairman.

Chairman TOM DAVIS. Thank you very much. Is there anything else anybody wants to say that maybe you didn't get in or respond to some other question? If not, great panel. We appreciate everybody's time, your testimony, and answering the questions from the members, too.

We will take about a 2-minute recess while we change the name tags and get our next panel up. Thank you.

[Recess.]

Chairman TOM DAVIS. I am going to start. I have to swear everybody in on our next panel. I want to thank our witnesses for appearing today. We have Dr. Robert Stroube, the Virginia State health commissioner. Dr. Stroube and I go back many years. In fact, your late father George helped me launch my political career back in 1979, when I ran for the board of supervisors, and then we worked together in Fairfax when I was chairman of the county board. And we are just very pleased to have you here today, and very proud of the job you are doing for the Commonwealth. You will be testifying on behalf of the Association of State and Territorial Health Officials to provide an assessment of State and local public health departments' ability to respond adequately to a public health threat.

We have Ms. Karen Miller from the National Association of Counties [NACo], who will provide the perspective from county and local health officials on preparedness.

We also invited three flu vaccine manufacturers to discuss vaccine production capacities and pandemic planning. Mr. Howard Pien, who is the president and CEO of Chiron Corp.; Dr. James Young, president of research and development at MedImmune will be joining us. Unfortunately, a representative from Aventis Pasteur was unable to attend, but the company has submitted written testimony for the hearing record. And, finally, Dr. Shelley Hearne, the executive director of the Trust for America's Health, produced a noteworthy report that provides an assessment of improvements to the public health system and remaining vulnerabilities.

We welcome all of you today. We are just really excited to have you.

It is the policy of the committee that all witnesses be sworn in, so if you would stand with me and raise your right hands.

[Witnesses sworn.]

Chairman TOM DAVIS. Ms. Miller, do you have somebody behind you who may answer questions?

Ms. MILLER. Dr. Susan Allan, who is the health director for Arlington County, VA.

Chairman TOM DAVIS. Oh, great, Susan. I am an old Arlingtonian of Cherrydale. That is where I went to elementary school.

Ms. MILLER. It is still Arlington.

Chairman TOM DAVIS. I know. Not in my district, but probably for the better, looking at their voting patterns.

Let the record show that you are here and sworn in as well.

Dr. Stroube, why don't I start with you, and I will move straight on down the line? And, again, thanks for being with us.

STATEMENTS OF DR. ROBERT STROUBE, VIRGINIA STATE HEALTH COMMISSIONER, ASSOCIATION OF STATE AND TERRITORIAL HEALTH OFFICIALS; KAREN N. MILLER, PRESIDENT, NATIONAL ASSOCIATION OF COUNTIES, COMMISSIONER, BOONE COUNTY, MO, ACCOMPANIED BY DR. SUSAN ALLAN, HEALTH DIRECTOR, ARLINGTON COUNTY PUBLIC HEALTH DIVISION, DEPARTMENT OF HUMAN SERVICES; HOWARD PIEN, PRESIDENT AND CHIEF EXECUTIVE OFFICER, CHIRON CORP.; DR. JAMES YOUNG, PRESIDENT, RESEARCH AND DEVELOPMENT, MEDIMMUNE, INC.; AND DR. SHELLEY A. HEARNE, EXECUTIVE DIRECTOR, TRUST FOR AMERICA'S HEALTH

Dr. STROUBE. Thank you, Mr. Chairman. Mr. Chairman and distinguished members of the House Government Reform Committee, I am the State health commissioner for the Virginia Department of Health and I will be testifying before you today on behalf of ASTHO, the Association of State and Territorial Health Officials. I would like to thank the Chair and the committee members for convening this hearing on a very important public health topic: emergency preparedness and our current capacity to respond to an influenza pandemic.

Substantial congressional investment in preparedness for public health has significantly aided our ability to rebuild Virginia's public health system. The Health Department in Virginia has become a 24/7 response agency and is now a key part of the State's homeland security infrastructure. This funding is being used to help prepare Virginia's public health and hospital system for a rapid and effective response to any event, whether it is bioterrorism, a naturally emerging infectious disease such as SARS, a new strain of flu, or a natural disaster such as hurricane. In order for Virginia to continue with the ongoing critical enhancement of its response capabilities, sustained funding from Federal grants is essential.

This funding has enabled Virginia to enhance and improve public health preparedness and planning, infectious disease surveillance and investigation, the State's public health lab, its communication technology, education and training, and health information dissemination. In addition, it has enhanced our ability to develop our State's smallpox preparedness programs and our ability to distribute the Strategic National Stockpile.

The President's 2005 budget proposal includes a $105 million cut from the CDC preparedness State grant funding. ASTHO opposes this proposal. Because no State or community is yet fully prepared, direct funding to the States for preparedness activities must be maintained at the current level provided in fiscal 2004 funding. The current proposed cut in funding would result in significant cuts in both State and local preparedness activities. The proposed cuts could jeopardize our ability to respond to a terrorist event, an outbreak of infectious disease, or other public health threats or emergencies. At a time when States are being asked to expand their role in disease surveillance and emergency preparedness, such a cut will jeopardize their ability to protect the public we serve.

In Virginia, such a cut in funding will reduce our current progress toward upgrading and enhancing our communication and

information technologies. Public health technology infrastructure has faced serious neglect for many years due to lack of funding. The Federal grant funding has enabled us to begin to rebuild our vital information technology system, which is a process that cannot be completed within just the 2 years that we have had grant funding. Our recent response to Hurricane Isabel, to SARS, the recent anthrax scare, and the early flu outbreak have demonstrated the importance of reliable and redundant communication systems. Once the information systems are established, they must be continuously maintained and upgraded as technology evolves. Such a funding cut also would impact our State laboratory, which still is in the midst of upgrading equipment to provide the most sophisticated methods available for rapid detection of biological and chemical agents. A Federal funding cut could also impact Virginia's ability to provide the best and most comprehensive training available for health care providers and emergency responders on biological, radiological, and chemical agents. For a State the size of Virginia, new training technologies, such as distance learning, are essential. Funding cuts could impact the health department's ability to provide education and training programs, which are necessary to ensure our response work force is always knowledgeable about the latest science.

With regard to unspent grant funds, it is important to know that any delays in spending of grant funding are due to the difficulties of hiring such a large quantity of highly qualified staff in such a short period of time. In addition, large expenditures have now been obligated for upgrades in highly sophisticated technology equipment. Virginia went to great lengths to properly research available systems prior to making decisions about what to procure. We also worked closely with other State and local emergency responders to ensure that we made wise purchases. Virginia is ensuring that its funding is being utilized to purchase technology that will effectively serve multiple purposes and correspond with its local emergency response partners' communication systems.

The current influenza season has certainly been a challenge for Virginia. The Governor, last summer, ordered an aggressive campaign to encourage flu vaccination in the State. We provided more than double the number of flu shots that we typically provide through our local health departments. This year we administered more than 160,000 doses of flu to members of the public. During a more typical year, the health department provides about 70,000 doses of flu vaccine.

While the Advisory Committee on Immunization Practices recommended that over 185 million people be vaccinated, only 87.1 million doses of vaccine were produced. However, this season we had an aggressive flu campaign and an early outbreak of flu. The situation was enhanced by extensive media coverage and heightened public awareness and demand for flu vaccine. The result was the available supply was unable to meet the demand. Public health worked to promote vaccination. Our efforts were undermined when the supply was inadequate.

In Virginia, many high-risk patients went without vaccine, parents could not get young children vaccinated, and health care providers could not vaccinate their staff. Attempting to prioritize vac-

cine to high-risk patients was a local health department nightmare. In some cases security was needed to maintain crowd control with demanding patients.

The present system of vaccine production and distribution was incapable of effectively responding to demands placed on it during the past flu season. While CDC, Virginia, and other States struggled to redirect vaccine supply, the reality was that people went unvaccinated.

Today, only three companies produce flu vaccine for the United States. Two of these companies produce inactivated, injectable flu vaccine and the third company produces nasal flu vaccine, which cannot be used for high-risk patients currently. Congress needs to support the development of a more reliable vaccine production process. The current system is incapable of meeting increasing vaccine demands or timely adjustment to the vaccine formulation. A review of the Nation's influenza program must include a comprehensive and critical look at all aspects of the system, including the production and distribution of vaccine.

Last, I would like to commend the leadership we receive daily from CDC. Whenever we have any kind of infectious disease outbreak, CDC provides rapid, clear, and concise communications and guidance. This communication is provided to the State through conference calls, through their continuously updated Web site, and publications such as the MMWR. CDC guides public health policy and provides critical guidance documents needed by both State and local health departments. In addition, CDC provides routine and accessible updates on information during public events as it becomes available and is a ready resource to the States through their emergency operation center.

In closing, I wish to thank Congress for the preparedness funding it has provided over the last 2 years. It has been essential for rebuilding the public health infrastructure in this country, but this cannot be seen as a short-term investment. Decades of neglect of our Nation's public health infrastructure make continued Federal investments necessary. We are eager and ready to address any public health emergency that may emerge in the coming years, but we are looking to you to ensure that we have the resources we need to protect the health of our citizens.

Thank you for the opportunity, and I would be glad to answer questions.

[The prepared statement of Dr. Stroube follows:]

Statement of Robert B. Stroube, M.D., M.P.H
State Health Commissioner
Virginia Department of Health

Before the House Government Reform Committee
On public health preparedness and the influenza season

February 12, 2004

Mr. Chairman and distinguished members of the House Government Reform Committee, my name is Dr. Robert Stroube. I am the State Health Commissioner for the Virginia Department of Health, and I am honored to be testifying before you today on behalf of the Association of State and Territorial Health Officials (ASTHO). I would like to thank the Chair and the subcommittee members for convening this hearing on a very important public health topic – emergency preparedness and our current capacity to respond to an influenza pandemic.

As State Health Commissioner I serve as the principal advisor to Virginia Governor Mark Warner, Virginia Secretary of Health and Human Resources Jane Woods and the Virginia General Assembly on a wide range of public health issues. I was appointed by Governor Warner in 2001. I have served Virginia in virtually every leadership position within public health at the state and local level during my career of nearly 30 years.

I earned a Doctor of Medicine degree from the Medical College of Virginia, a Masters in Public Health from the Johns Hopkins University, and an undergraduate degree from the College of William and Mary. I am a specialist in preventive medicine and certified by the American Board of Preventive Medicine.

Introduction

Public health has taken a dramatic turn since the Pentagon and anthrax attacks of 2001. Those events brought to light the long-time deficiencies within our nation's public health infrastructure for a rapid response to emergencies that impact the health of our citizens. Over the last several years funding and support for public health steadily declined leaving a system seriously lacking the capacity to manage emergencies in real-time.

The substantial congressional investment in preparedness for public health has significantly aided in our ability to not only rebuild Virginia's public health system but also transform the health department into an emergency response agency. The funding is being used to help prepare Virginia's public health and hospital system for a rapid and effective response to any event, whether it is bioterrorism, a naturally emerging infectious disease, such as SARS, a new strain of influenza, or a natural disaster, such as a hurricane. In order for Virginia to continue with this ongoing critical enhancement of our response capabilities, sustained funding from federal grants is essential.

Funding Allocations

In 2002, the Virginia Department of Health (VDH) received more than $25 million in federal funding for public health and hospital preparedness. For the 2003-2004 funding period, VDH received $37 million in federal grant support.

The federal grants include $19.5 million from the U.S. Centers for Disease Control and Prevention (CDC) for public health preparedness and $11.8 million from the U.S. Health Resources and Services Administration (HRSA) for hospital and health system preparedness, mental health services and to address the needs of special populations. The HRSA funds are helping to enhance hospitals' capacity to respond to mass casualty incidents requiring mass immunization, treatment, isolation and quarantine in the aftermath of bioterrorism or other outbreaks of infectious disease, provide mental health services and address the needs of special populations.

In addition, VDH received an estimated $2.4 million from CDC for smallpox preparedness efforts, $1.5 million from the U.S. Department of Homeland Security for the Strategic National Stockpile, and $1.5 million to the state laboratory for enhancement of chemical agent testing capabilities.

The funding coming to VDH through the CDC has enabled Virginia to enhance public health preparedness and planning, improve infectious disease surveillance and investigation, advance the state's public health laboratory and communication technology capacity, provide education and training, and enhance health information dissemination. This year the funding also will address the continued development of the state's smallpox preparedness programs, and enhancement of the state's abilities to distribute the Strategic National Stockpile.

Despite uncertainty about the continuation of this level of funding, Virginia determined that the best use of these funds was to hire highly qualified public health staff at the state and local level to bolster our capacity to respond to any emergencies. In addition, Virginia decided from the beginning to take an all hazards approach with the use of the funding in order to enhance our ability to respond to any public health threat – not just bioterrorism.

To date, Virginia has hired more than 140 new public health and health care personnel with the funding including physicians, emergency planners, disease outbreak investigators, trainers, technical staff, laboratory specialists, hospital coordinators and public information officers throughout the state.

The new public health personnel hired with the grant funding are working on preparedness issues throughout Virginia at the local, regional and state level. Each of Virginia's 35 local health districts hired one emergency response planner and one epidemiologist for a total of 70 people contributing to local health department work force capacity.

In addition to hiring local public health personnel, Virginia established five regional emergency preparedness and response teams. Most of the teams include a physician consultant, epidemiologist, emergency planner, training coordinator and public information officer. The team's role is to facilitate regional coordination among the local health districts, hospitals and local jurisdictions and augment local resources during an event. The regional public health response teams are available to respond to any area of the state when an emergency event begins to unfold. This is a vital workforce resource that our health department would never have been able to establish without the federal funding.

Prior to the federal funding, our disease investigation unit was severely under staffed. The total team for the state's disease investigation division consisted of about 11 people who were responsible for monitoring in excess of 12,000 morbidity reports per year for Virginia. With the federal funding many new state office positions have been established including a medical epidemiologist, nurse epidemiologist, surveillance chief, statistical analyst, database manager, a bioterrorism surveillance coordinator, two senior epidemiologists, and a program support technician.

Increasing our epidemiologic capacity at the state level has resulted in an improved ability to: develop emergency response plans (e.g., for pandemic influenza, smallpox and SARS), develop disease guidance documents for healthcare providers, respond to disease outbreaks, assess morbidity and mortality from communicable diseases, enhance surveillance of reportable diseases, and provide strong guidance to local health departments regarding surveillance and investigation of diseases and emerging public health threats.

The hiring of an epidemiologists within each local health department has improved response time to disease reports, timeliness and completeness of disease reporting, and it has enabled health departments to respond better and faster to public health emergencies, such as the recent hurricane and the SARS epidemic. These are important roles that have allowed VDH to meet critical public health needs daily to control communicable diseases in our communities.

But the positions alone are not all that is needed to ensure a successful public health response. Providing continuous education and training to public health personnel and other health care providers is essential. The federal grant funds have provided for the development of specialized orientation sessions, new on-line education programs and collaborative instruction efforts. Our emergency preparedness training and education team is utilizing distance learning technologies such as video conferencing, satellite broadcast and the internet to provide public health personnel and health care professionals training on issues, including smallpox vaccination, management of newly emerging infectious diseases and incident command operations.

The federal grant funding has provided for greatly needed upgrades to many of the health departments' information technology systems, which are fundamental for an effective response to any emergency event. For example, all key public health emergency

preparedness personnel — from state planners and epidemiologists to key central office staff — are outfitted with sophisticated pagers and laptops for instant access and around-the-clock availability. The federal grants have supported purchase of this wireless equipment, as well as upgrades in e-mail systems and back up communication systems.

The health department's existing Health Alert Network is currently being upgraded to enhance the rapid relay of critical health care information to the health community and all levels of government. With the upgrade in place, a warning could be forwarded more rapidly from VDH to local health departments and health care providers across the state.

In addition, the health department's information technology team, supported with federal grant funding, is building a computer-based infrastructure designed to rapidly collect, analyze, and present data from a number of different healthcare sources to determine possible disease outbreaks, including bioterrorism.

State Laboratory

The state public health laboratory has had great difficulty hiring scientists to work in containment laboratories, both the biological safety level 3 (BSL-3) and the chemical terrorism laboratories. They also have had difficulty hiring highly qualified personnel to do the rapid and specialized molecular assays such as real time polymerase chain reaction (PCR) which can provide a diagnosis within 30 to 40 minutes versus the usual three to four days for bacteria and up to two weeks for virus cultures. We must improve efforts to recruit young people to enter the sciences, provide laboratory training to the most promising students, and then provide incentives for working in public health. A shining star is the Emerging Infectious Diseases Fellowship Program sponsored by CDC and Association of Public Health Laboratories (APHL) which provides young scientists with hands-on training in public health laboratories.

Public health laboratories offer a great training ground for scientists, but have difficulty paying the salaries necessary to retain the best and brightest. Without sustained federal funding, we would lose most of the personnel we have trained on the sophisticated laboratory methods needed for emergency preparedness testing in a public health laboratory. About 15 percent of our laboratory workforce is paid by federal funds, and as many as 30 percent of our highly trained technical personnel are federally funded.

Due to these difficulties in recruiting and hiring laboratorians and epidemiologists, some of the federal grant funding was available at the end of the grant year. Those carryover funds were not wasted. They were used to purchase much needed major equipment, including the laboratory equipment needed to safely contain potentially hazardous materials in unknown samples while they are being analyzed.

The recent onset of the highly pathogenic avian influenza virus H5N1 in several countries in Southeast Asia and the high mortality in associated human cases has raised awareness of influenza. Although the laboratory has some high containment facilities, it does not yet have the ability to diagnose H5N1 flu because it still does not have laboratories at the

higher bio-containment level needed to safely grow highly pathogenic avian flu or the SARS human coronavirus. Also, reagents to test specifically for the H5N1 virus using non-culture methods have not yet been made available from the CDC. Therefore, continued support for both the CDC and the state public health labs is necessary so that we can be "pandemic flu ready."

The laboratory has developed strong working relationships with federal agencies (FBI, CDC, EPA, DOD, FDA, USDA, and others in the Capitol region). These relationships have benefited citizens of the Commonwealth and of neighboring states by providing quick access to laboratory services during an emergency, as well as safer working conditions for the people collecting and handling hazardous substances.

Importance of CDC State Preparedness Grant Funding

The President's Fiscal year (FY) 2005 budget proposal includes a $105 million dollar cut from the CDC Preparedness state grant funding. ASTHO opposes this proposal. Because no state or community is as yet fully prepared, direct funding to the states for preparedness activities must be maintained at least at the level of the current FY 2004 funding. The current proposed cut in funding would result in significant cuts in state and local preparedness activities. The Administration's proposed cuts could jeopardize our ability to respond to a terrorist event, outbreak of an infectious disease or other public health threats or emergencies. At a time when states are being asked to expand their role in disease surveillance, and emergency preparedness, such a cut will jeopardize our ability to protect the public we serve.

In Virginia, such a cut in funding will reduce our current progress towards upgrading and enhancing our communication and information technologies. Public health technology infrastructure has faced serious neglect for many years due to lack of funding. The federal grant funding has enabled us to begin to rebuild our vital information technology system, which is a process that can not be completed within just two years. Our recent response to Hurricane Isabel, suspect cases of SARS, the recent anthrax scare and the early flu season demonstrated the importance of reliable and redundant communication systems. Once new information systems are established, they must be continuously maintained and upgraded as technology evolves. Such a funding cut also would impact our state laboratory, which is still in the midst of upgrading equipment to provide the most sophisticated methods available for rapid detection of biological and chemical agents. A federal funding cut also could impact Virginia's ability to provide the best and most comprehensive training available for health care providers and emergency responders on biological and chemical agents. For a state the size of Virginia, new training technologies, such as distance learning are essential. In addition, funding cuts could impact the state health department's ability to continuously provide education and training programs, which is necessary to ensure our response workforce is always knowledgeable about the latest science.

In regards to unspent grant funds, it is important to note that any delays in spending grant funding were due to the difficulties of hiring such a large quantity of highly qualified

staff in such a short period of time. In addition, large expenditures have now been obligated for upgrades in highly sophisticated technology equipment. Virginia went to great lengths to properly research available systems prior to making decisions about what to procure. We also worked closely with other state and local emergency responders to ensure that we made wise purchases. Virginia is ensuring that our funding is being utilized to purchase technology that will effectively serve multiple purposes and correspond with our local emergency response partner's communication systems.

Importance of HRSA Funds

The President's Fiscal year (FY) 2005 budget proposal includes $476 million nationally for the bioterrorism hospital preparedness program under HRSA. The FY05 budget covers the fourth year of the hospital grant program. This represents a $39 million reduction from the (FY) 2004 budget.

If funding from the HRSA grant for Virginia is reduced, progress in priority areas, such as surge bed capacity, clinical personnel augmentation, isolation capacity and hospital-based pharmaceutical caches will be adversely affected.

The funding is greatly needed to provide additional capacity in the event of a sudden surge in patient demand. Meeting this surge in patient demand requires enhancement of internal hospital plans including conversion of auxiliary areas and acquisition of portable cots and accessories; enhancement of hospital diversion and patient transport protocols utilizing Web-based resource tracking systems; identification of alternative care sites with costs of acquisition and/or renovation and equipping and recruitment of trained Medical Reserve Corps volunteers. A cut in funding would inhibit our efforts to maintain the expected level of reserve capacity.

Funding for acute care hospital increase of isolation capacity and upgrade of existing air handling and filtering is crucial. It is especially important in order to avoid hospital emergency rooms from being contaminated and prevent contamination throughout the hospital. A cut in funding would likely reduce the number of hospitals in which the emergency room could be isolated and contaminated patients could be examined and treated.

Protection of our hospital healthcare workers is one of our first lines of defense. If nurses, doctors and support personnel are incapacitated by the first wave of infected incoming patients or by direct exposure to an agent, the results would be catastrophic. Therefore, an adequate supply of prophylactic pharmaceuticals must be on hand or readily available for hospitals to use to protect staff and patients.

Exercising Plans

Both grants require regional and statewide exercises to test and evaluate health department and state emergency plans. Virginia made the decision to have a full scale statewide bioterrorism exercise that would involve a broad range of agencies and

organizations that may be involved in responding to a bioterrorism event. All of the state's 35 local health districts, state health department, state laboratory, Chief Medical Examiner, hospitals, the Strategic National Stockpile (SNS) team from the CDC, the state emergency management agency and multiple other state and local agencies participated in the exercise in October 2003.

While participating groups were aware of the general scenario and timing of the exercise, the biological organism and public event where exposure occurred were not known to most exercise participants. Patients with respiratory symptoms were first presented to hospitals statewide on October 19. Eighty-percent of the hospitals in Virginia participated in the exercise. Local epidemiologists throughout the state were contacted by their local hospital to report the occurrence of an unusual illness. The recognition of the outbreak immediately prompted a statewide epidemiologic investigation.

The exercises tested abilities to isolate cases at hospitals, collect and transport samples for testing at the state laboratory and coordination with the medical examiner who was managing a large number of mock casualties during the exercise.

The outbreak was identified as a college alumni dinner with alumni returning home to areas throughout the state. Once the outbreak was identified, the SNS push-pack was requested on day two of the exercise and it arrived on day three. The biological organism causing illness was identified as the *Yersinia pestis*, the bacterium that causes plague, and decisions about treatment and preventive treatment were made.

During the exercise the VDH Emergency Coordination Center (ECC) was opened. The SNS push pack arrived in Richmond and was transported to hospitals and dispensing sites in all six regions of Virginia. More than 2,200 volunteer patients presented at the dispensing sites to receive preventive medications or vaccinations.

The City of Richmond and the health departments in far southwest Virginia used this opportunity to test their capacity to provide mass vaccinations. In Richmond, buses brought in nearly 500 elderly people from public housing communities to provide them with an actual flu vaccine. In far southwest Virginia, 152 volunteers received the flu vaccine as they were processed through the dispensing site.

VDH partnered with various federal, state and local emergency partners to conduct this exercise and test communications between the agencies. VDH worked cooperatively with state agencies to manage the site in Richmond where the pharmaceuticals are received, broken down and then distributed statewide to our local health departments.

For example, the Virginia Department of General Services provided the warehouse for receipt of the SNS, as well as staff to unload, repackage and reload portions of the stockpile for distribution to the six regions by a private delivery service. State police provided security for the warehouse and local police provided security for each dispensing site. The CDC sent representatives to observe our processes during the exercise, and the management of the SNS was judged to be exemplary by the CDC.

Dispensing site activity was successful but issues of staffing, security and resources still need to be resolved.

The result of the exercises, which was funded entirely by our federal grant, provided a wealth of training for staff and identified strengths and weaknesses in our response plans. The cost for conducting this exercise was kept to a minimum ($30,000) because all planning and most implementation was done by VDH, the state laboratory and other state employees, many of whom were funded through CDC and HRSA grants.

Exercising such events is the only way we can test our plans, identify our weaknesses and continue to enhance our systems. This was the first time VDH conducted a statewide exercise involving an infectious agent. Our grant funding will provide for annual statewide exercises and annual regional exercises, which will continue to strengthen our capabilities. In addition to the state exercise, five regional exercises were also completed last year, and health department staff also participated in other numerous local emergency responder exercises.

One particular local exercise that I would like to note was lead by Arlington Health Department. The exercise conducted earlier last year involved a smallpox mass vaccination clinic. This was the first real opportunity for local, state and federal partners to identify actual costs and workforce hours such a clinic will demand. The exercise was a huge success, and the lessons learned from the event were extremely valuable.

Real Events

Real events this past year have also tested our newly enhanced capabilities. For response to Hurricane Isabel, VDH opened its own Emergency Communication Center ECC within the agency to manage the flow of information and requests for public health resources coming to and from our state Emergency Operations Center. The increase in public health staff due to the grant funding enabled VDH to respond to the hurricane with a full staffing of the agency's ECC 24/7 to ensure rapid response to all public health needs.

VDH responded to a wide-variety of public health issues prior to, during and following Hurricane Isabel. The VDH Chief Medical Examiner's Office tracked 33 hurricane-related deaths in Virginia. The VDH Office of Epidemiology collected daily injury report information from 18 hospitals in the Northern, Eastern and Central regions 10 days prior to and following the hurricane. VDH also monitored hospital and life-line facility (e.g., acute care, nursing home) power restoration efforts, water and oxygen supply needs.

Following the hurricane, VDH in cooperation with the Virginia Department of Emergency Management and the Federal Emergency Management Agency conducted aerial spraying for mosquitoes from low flying aircraft in localities that were at increased risk for mosquito borne disease due to increases in mosquito populations.

In addition, hundreds of boil water advisories were issued by waterworks systems throughout the state due to power loss or flooding issues. Approximately 71 percent of restaurants in Virginia were impacted, about 16,700 restaurants. A significant amount of health department resources were utilized to visit or contact restaurants in areas where power failure occurred or where there were boil water advisories. Health department inspectors provided guidance on how and when restaurants could reopen for business.

Other areas in which health department resources were employed during the hurricane include our Emergency Medical Services (EMS) task forces, which were deployed to different areas to assist local EMS teams. The dissemination of timely and accurate health information to our citizens prior to, during and following the storm was also very important in order to inform citizens of the necessary steps needed to protect health.

Based on the lessons learned from both the hurricane and the exercise, a multidisciplinary committee has been established with a charter to develop changes to policy, training, planning, techniques, procedures, facilities, equipment, and communications. Recommendations from this committee will then be used to modify both the VDH and state Emergency Operations Plans. This process will be completed by August, 2004 when Virginia will be a major participant in the national Department of Defense exercise, Determined Promise 2004.

In addition, VDH has responded recently to infectious disease situations including the emergence of Severe Acute Respiratory Syndrome (SARS). Last year, VDH evaluated 69 persons reported with symptoms compatible with SARS. The evaluation of each of these cases requires an intensive investigation to determine relevant travel history, symptoms, and rule out diagnoses. If a case was considered suspect after this initial investigation, local health department epidemiologists hired under our federal grant worked closely with hospitals to insure the proper infection control procedures were being followed. For the patients, local public health staff had to give recommendations for isolation so that others would not be exposed and infected. Specimens also had to be collected for laboratory confirmatory testing. Public health staff also identified close contacts of the patient and monitored all contacts for development of fever or respiratory symptoms for 10 days. Monitoring the close contacts was very important to ensure that those exposed to the patient didn't develop symptoms consistent with SARS and further spread disease in the community.

A striking example of how the federal grant funding has provided Virginia with a dramatically increased ability to deal with unknown agents is the impressive service our state public health laboratory was able to provide during the SARS outbreak. CDC very quickly developed rapid diagnostic assays and provided the methods and reagents to the state public health laboratories. Thanks to the funding, our laboratory had the highly sophisticated instruments and trained personnel to implement these methods and provide rapid diagnostic tests for SARS within just a few months of the discovery of this completely new human pathogen.

Another example of an actual situation that tested our abilities to detect and respond was the unexplainable and sudden deaths of five children in a five day period last year in Virginia. The Medical Examiner's office quickly recognized this unusual occurrence and quickly notified myself and our disease surveillance and investigation division. A full-scale epidemiologic investigation immediately began in both the Hampton Roads and Richmond area to determine if there was any link among any of the cases.

VDH worked cooperatively during that incident with Homeland Security, Federal Bureau of Investigation, Secretary of Health and Human Services command center, U.S. Department of Agriculture, U.S. Environmental Protection Agency, and other federal organizations. Although VDH did not believe this incident was terrorist related, we went to great lengths to rule out terrorism. We even worked with our state laboratory to have scientific tests for biological and chemical agents run through the middle of the night.

In the end, some of the tragic deaths were determined to be due to influenza and none of the cases were connected. But had this been an actual terrorism incident or a naturally occurring outbreak of disease, we feel confident that we were prepared to meet that challenge due to our rapid detection and response to the situation.

Smallpox Preparedness

Another large effort this past year was developing Virginia's smallpox program. After 30 years of dormancy, the smallpox vaccine is now being provided to those that might respond to a smallpox case or outbreak. Launching this new program required a great deal of coordination and effort. Including the implementation of a statewide education and training program regarding smallpox recognition, containment and vaccination techniques to prepare healthcare professionals for swift and effective response to a potential outbreak.

Local public health staff dedicated many hours to organize and establish smallpox vaccination clinics to provide the vaccine to volunteer health care professionals. To date, Virginia has vaccinated 883 people including public health, hospital, emergency responders and federal law enforcement personnel.

A comprehensive Smallpox Response Plan was developed and is being incorporated into the VDH Emergency Response Plan. This year the smallpox vaccination program will expand to provide educational training to additional hospital staff and other health care providers that would be utilized during an event to provide vaccinations or care to the public.

Influenza

This recent influenza season was certainly a challenge for Virginia. VDH provided more than double the number of flu shots than is typically provided through our local health departments. This year VDH administered more than 160,000 doses of flu vaccine to members of the public. During a more typical year the health department provides about

70,000 doses of flu vaccine. It is important to know that public health provides a small percentage of the flu vaccine to the general public compared to the vaccine supplied in the private sector.

While the Advisory Committee on Immunization Practices recommended that over 185 million persons be vaccinated, only 87.1 million doses of vaccine were produced. This includes approximately four million doses of nasal vaccine (Flumist) which could not be used to meet the needs of high-risk patients. In a typical flu season this level of production may be adequate since fewer than half of the 185 million people for whom CDC recommends a flu shot usually get one.

However, this season we had an aggressive flu vaccination awareness campaign and an early flu season. The situation was enhanced by extensive media coverage, heightened public awareness and demand for flu vaccine which stretched well into December and January. The result was that the available supply was unable to meet this demand. Public health worked to promote vaccination and our efforts were undermined when the supply was inadequate.

In Virginia, many high-risk patients went without vaccine, parents could not get young children vaccinated, and healthcare providers could not vaccinate their staff. Attempting to prioritize vaccine to high-risk patients was a local health department nightmare. In some cases security was needed to maintain control of demanding patients.

VDH epidemiologists conducted surveillance for cases of flu-like illness and complications such as pneumonia, mental status changes, and death. VDH also worked intensively to provide information on means of preventing the spread of influenza and information on the vaccine supply to medical providers, schools, nursing homes, and citizens.

The present system of vaccine production and distribution was incapable of effectively responding to the demands placed on it during this past flu season. While CDC, Virginia and other states struggled to redirect vaccine supply, the reality was that people went unvaccinated.

Today, only three companies produce flu vaccine for the U.S., and only two of these companies produce only inactivated injectable flu vaccine. The third company produces the nasal flu vaccine, which cannot be used for high-risk patients. Congress needs to support the development of a more reliable vaccine production process. The current year-long process is incapable of meeting increasing vaccine demands or timely adjustment to vaccine formulation. A review of the nation's influenza program must include a comprehensive and critical look at all aspects of the system including production and distribution of vaccine.

The experience this past year managing an early influenza season does cause concern for possible occurrence of an influenza pandemic in the U.S. The CDC guidance on planning for pandemic influenza is good, but is still in draft form and has been for years.

A pandemic influenza planning checklist developed by the ASTHO has also provided a basis for state response plans.

Virginia developed a pandemic influenza plan in June 2002, but challenges for implementing the plan remain. More communication with the public and private healthcare community is needed to ensure the workforce is aware of the plan and the implications of its contents. Further training on the plan and exercising the roles of each individual are also essential.

In a pandemic influenza situation, hospitals would quickly be overwhelmed and would require additional resources, too. There would be a need for staffed beds; infection control supplies such as masks, ventilators, and negative pressure rooms; emergency department beds and staff; separate triage areas for patients with respiratory symptoms, etc. We can anticipate shortages in these areas. Shortages would also be expected in morgues and other post-mortem services. Laboratory resources would also be crucial.

In a pandemic, there would be a significant demand for public information and real-time statistics. It would require resources to devote to these items. For example, public health would be expected to know the number of persons ill, the number hospitalized, the number breathing on ventilators, the number experiencing complications such as pneumonia and confusion, and the number dying. Hospitals would likely be too short staffed to provide these data, so public health resources would be needed to gather the information on a daily basis. Gathering these data from multiple facilities and jurisdictions is a complicated process. This would divert the limited staff from other public health prevention and control responsibilities.

The data will also be vital for the difficult decision making processes, such as prioritizing who could receive the potentially limited supplies of vaccine and antiviral medications, and who could use the limited hospital beds and ventilators available.
Making such complex decisions will depend on viable data concerning the population groups at risk for illness, complications, and death. Thus, we will have a valid policy reason to devote resources for collecting detailed information about the occurrence of illness and its complications.

The nation's infrastructure could be threatened in a pandemic situation due to worker absenteeism. This could occur not only in schools and healthcare settings, but also within utilities and other needed sectors. Businesses could also be threatened due to people avoiding public places, such as shopping malls and theaters.

It will be difficult, if not impossible, to have enough resources available to respond to such a large scale outbreak. This is why it is imperative that at a minimum we maintain the public health workforce currently supported by our federal grant funding.

Every day disease situations arise that give real-life experience to newly hired and veteran public health practitioners that will help them respond to occurrences on a larger scale. This infrastructure is critical to protecting our public's health.

In Virginia alone, we estimate that during an influenza pandemic we could have over 1.3 million outpatient visits, over 28,000 hospitalizations, and over 6,200 deaths in a 12 week period.

We will need about 180,000 hours of public health provider time to vaccinate the high-risk population alone. More time would be needed if the vaccine was not approved by the FDA or if more people than just those at high-risk were immunized. In addition, we would need to monitor for side effects of the vaccine, adverse events associated with antiviral medications, and complications of the illness itself.

Immunization Policy

In regards to immunization policies, the difficulties of providing a large scale adult vaccination program for a response to influenza are immense. Currently, the focus is on providing childhood immunization programs and coverage levels are at an all time high.

However, since 1999, the vaccine purchase appropriation has increased by 50 percent while the cost of immunizing a child for all recommended vaccines has increased by over 125 percent. This level of funding not only jeopardizes the gains made in childhood immunization, but has resulted in Virginia being unable to provide the Standard of Care to all children equally. Funds are currently not available for the provision of pneumococcal vaccine for children other than those eligible for the Vaccines for Children Program. The current level of funding minimizes the efforts that can be made at improving the delivery of immunization services to adults.

The (FY) 2004 Omnibus funding bill recently passed by Congress that further reduces domestic vaccine purchase by $3 million will compromise the integrity of an already under-funded childhood immunization initiative and make it impossible for States to effectively expand adult immunization efforts, which includes influenza preparedness. Consideration should be given to amending the present Vaccines for Children Program (VFC) legislation to authorize the provision of VFC vaccine to underinsured children by all enrolled providers. The present law limiting the provision of VFC vaccine to the underinsured to Community Health Centers has resulted in the expenditure of limited State and 317 funds to meet the needs of this group. The $3 million reduction in Section 317 funds from (FY) 2003 to (FY) 2004 and as recommended in the President's budget for (FY) 2005 will damage immunization efforts. Additional funds are needed to ensure that all states provide pneumococcal conjugate vaccine (PVC-7) in their immunization programs. Virginia along with 18 other states currently does not provide this vaccine. Additional funding is also needed to cover the pediatric influenza vaccine recommendations.

CDC leadership

Lastly, I would like to comment on the commendable leadership provided daily by CDC and during any infectious disease outbreak response. VDH depends on CDC for rapid, clear and concise communication and guidance. This communication is provided to the

state through conference calls, their continuously updated Web site, and publications such as the Morbidity and Mortality Weekly Report. CDC guides public health policy and provides a model for the creation of certain guidance documents needed at the state and local level. In addition, CDC provides routine and accessible updates on information during public health events as it becomes available and is a ready resource to States through their emergency operations center.

In closing, I wish to thank Congress for the preparedness funding it has provided in the last two years. It has been essential for the rebuilding of our public health infrastructure, but this cannot be seen as a short term investment. Decades of neglect of our nation's public health infrastructure make continued federal investments necessary. We are ready and eager to address any public health emergencies that emerge in the coming years, but we are looking to you to help ensure that we have the resource needed to protect the health of our citizens.

Thank you for this opportunity to speak with you today. I would be pleased to answer any questions you may have.

Appendix:
House Committee on Government Reform questions regarding influenza season and the Nation's preparedness to handle major public health threats.

1) What established planning procedures were in place at the state level to handle this year's influenza season or other communicable disease outbreak? Did state health officials need to take any additional actions or procedures to respond to the recent influenza season?

   Answer: Local health districts predicted* flu vaccine needs and pre-ordered supply in January 2003. Vaccine was received and distributed to all health districts and VFC providers by mid-September.
   As vaccine supply became depleted, the state health department rapidly identified under-utilized vaccine inventory and redirected supply to areas where needed. VDH contacted CDC to gain authorization to redirect unused VFC flu vaccine to non-VFC eligible patients. In addition, VDH had to quickly change its recommendations to target the most high-risk patients.

2) What approach are state health officials taking to educate the general public on influenza and vaccines or major public health threats? Have the recommendations the CDC have developed to prevent the transmission of influenza and other disease outbreaks proven to be effective?

   Answer: In Virginia, an extensive public awareness campaign has been underway to educate citizens about potential public health threats. VDH had an aggressive campaign to educate citizens about protecting against influenza by getting the flu shot. In addition, VDH has distributed information about public health

emergency preparedness to citizens through newspaper supplements, press release, media interviews and the Web.
CDC recommendations have been instrumental in educating and updating providers and sending one clear concise message. However, our vaccine campaign efforts were undermined when the supply was inadequate.

3) Which procedures were effective in preventing the spread of influenza among people who came into close contact with infected patients? Have you discovered any gaps in state planning and preparedness for an epidemic of a communicable disease?

Answer: Vaccination of the public prior to flu season is the best protection against influenza. Once flu vaccine was not available, VDH aggressively recommended respiratory etiquette tips, such as frequent hand washing, coughing into tissues, and staying home when sick.
The planning and preparedness gaps identified this year include our ability to handle patient surge capacity, the need for an enhanced healthcare provider alert system, and vaccine re-distribution procedures. Another challenge is the flow of useful and accurate information among federal, state and local agencies.

4) What are the potential resource needs of state public health systems for responding to communicable disease outbreaks, particularly airborne diseases and influenza? Does our Nation's public health system currently have the necessary resources to respond adequately to this type of public health threat?

Answer: Public health and hospital systems need a highly qualified and trained workforce in order to respond to communicable disease outbreaks. In addition, we need reliable and redundant communication technologies to support our response to any event. In Virginia, our public health system has made significant progress towards having adequate resources to respond to public health threats, but continued federal support of those resources through grant funding is needed to maintain this progress.

5) Has the federal government provided state jurisdictions with adequate guidance for planning and preparedness activities? Additionally, have federal, state and local jurisdictions developed mechanisms to evaluate and share best practices and strategies?

Answer: The CDC guidance on planning for pandemic influenza is good, but is still in draft form and has been for years. A pandemic influenza planning checklist developed by the ASTHO has also provided a basis for state response plans. More communication with the public and private healthcare community is needed to ensure the workforce is aware of the state's pandemic influenza plan and the implications of its contents. Further training on the plan and exercising the roles of each individual are also essential. In Virginia, best practices and evaluation procedures have been developed as a result of experiences from

Hurricane Isabel and our state exercise. Those best practices and lessons learned are being implemented into our plans and distributed to our partners.

6) What does our public health system's response to and readiness for the 2003-2004 influenza season say about the overall ability to respond to a pandemic?

Answer: The limitations of vaccine supply, the production process and the lack of flexibility within production process once a viral shift situation is identified all will make it very difficult to effectively respond to pandemic influenza. Although what is encouraging is that the public health system has proven this past year it can respond to the constantly changing dynamics of any situation if given the resources necessary.

7) Currently, how many states have developed an influenza pandemic plan? What is the status of these plans? What concerns exist at the state level regarding the federal role in funding and improving preparedness?

Answer: Since June 2002, Virginia has had an influenza pandemic plan. But in order to effectively implement the plan we need to continue our training, exercises and updating our plans. The biggest concern for state's regarding the federal role in funding is that level funding over a sustained period of time is necessary in order to keep public health agency's prepared and ready to respond.

8) What difficulties did state health officials experience in procuring influenza vaccines this year? How did state health officials handle the vaccine shortage? What steps and procedures can be taken now to avoid a shortage during the 2004-2005 year's influenza season?

Answers: The major difficulty in procuring flu vaccine this year was simply that there was not enough vaccine produced to meet demand. Virginia handled the vaccine shortage as best we could by ensuring that unused doses were identified and redistributed and that the restriction on unused VFC vaccine was lifted. Avoiding shortages again next year will require the production of more vaccine and the ability to response to changes in vaccine demand. The federal government needs to work with manufactures to manage the economies of scale issue that could arise if producing more vaccine results in un-purchased vaccine. In addition, we need more manufactures of injectable vaccine and existing manufactures need to be encouraged to maximize production.

Chairman TOM DAVIS. Thank you.

Ms. Miller.

Ms. MILLER. Good morning, Mr. Chairman. My name is Karen Miller. I am a commissioner in Boone County, MO, and also president of the National Association of Counties; and, as you know, NACo is the only organization that represents county governments at the national level. Additionally, I would especially like to thank the National Association of County and City Health Officials, whose expertise I use today in preparing this testimony.

America's 3,066 counties vary in geographic shape, size, population, and services they provide, but one common thread is that they all have an integral role to play in protecting our communities. Counties are the Nation's "first responders," responding to virtually every emergency situation, whether it is a flood, an act of terrorism, or an outbreak of disease.

Mr. Chairman, I have one overall message for you today. We have made much progress in public health preparedness, but we have along way to go. At the local level, the people who work diligently on influenza immunization are the same people who are working every day to improve public health preparedness for any type of emergency. As the public health threats to which they must respond increase, we are asking the same people to do much, much more with resources that still are very limited. Today, on behalf of the Nation's counties, I urge two actions: sustained and increased Federal funding for public health preparedness, and greater systematic attention by Federal policymakers to the realities of local public health emergency planning and response.

As this committee has recognized, our communities must be prepared for any disease outbreak, whether it results from an act of nature or an act of terror. We have all been concerned about the potential for widespread influenza, because we have seen how it can take the lives of our children. We remember the scares caused by the anthrax attacks of 2001, and we want to be sure we know what our communities will do if the unthinkable occurs.

The good news is that our Nation's counties are better prepared now than they were 2 years ago. The infusion of Federal funds for building State and local public health capacities has helped a great deal. The plans that are in place will serve us well, whether we face an outbreak of influenza or smallpox.

We have already benefited from improved public health preparedness, even though there has been no truly catastrophic event. For instance, although we hope we will never see a case of smallpox, we have made great progress in planning for mass vaccination.

In my own county, the work we did last year on developing a local health alert network, which was aided in part by public health preparedness grant funding, improved our response to influenza this year. It enabled us to share current local data about flu cases and State and CDC recommendations with our local medical providers. Our new grant-funded regional epidemiologist created weekly influenza summaries that we sent out to the medical community via the local Health Alert Network. This has improved physician reporting of influenza, which is essential to help us identify any large outbreak. A regional public health information officer, also hired with public health preparedness grant funds, serves us

and 16 other counties. This has enabled us to help be more proactive in educating the general public about flu vaccination and how to prevent the spread of flu.

However, when my health department, or other local health departments, need to respond to influenza, or to a requirement to vaccinate medical personnel against smallpox as we did last year, we are still using the same staff that carries out routine public health activities. The number of hours required to plan and carry out vaccination clinics pulls many people away from routine duties and those come to a halt. We just don't have the resources or the staff to compensate for these demands. Of the approximately 3,000 public health departments in the country, nearly all are understaffed and underfunded. What we want you to understand is that we have drawn upon far more local resources than Federal funds to move forward in the public health preparedness.

We still have a long way to go. We know that large-scale influenza or SARS might resurface in any community at any time. However, we have never had to implement large-scale isolation and quarantine. In addition, many communities are concerned that they lack adequate arrangements for what we call "surge capacity," that is, extra doctors, nurses, epidemiologic investigators, and others who are not needed all the time, but would need to be called into service to contain an outbreak and care for patients in an emergency.

It is essential that the Federal Government remember that public health preparedness is not a destination that some day we will reach and then be able to stop. Rather, it is a journey during which we will improve little by little, day by day and year by year. We must always be using exercises to test our abilities and we must always be training new people, adapting to new technologies, and preparing to address new threats.

Most local health departments had plans for identifying stocks of available vaccine and reallocating vaccine among providers in their community. The unexpected demand for flu vaccine and its subsequent unavailability concerned us because it required us to change our strategies and our public message midstream. It pained us greatly when we found ourselves unable to offer vaccination to all who asked, particularly because the FluMist vaccine that remained available is unsuitable for children and high-risk groups on whom we focus our service. There were approximately 70 counties in my State alone that experienced a flu vaccine shortage this year. Overstocking, though, is way too costly.

Public health requires good collaboration between Federal, State and local governments because each has an important, unique role to play. The fact remains, though, that disease outbreaks don't occur in States; they occur in communities. It is our counties and cities that bear the greatest burden for response. In addition, it is essential to understand that public health preparedness at the local level does not involve only our public health departments, it is an overall emergency management system with all the public and private partners.

In closing, I would like to reemphasize the need for sustained and increased Federal funding for public health preparedness and greater systematic attention by Federal policymakers to the reali-

ties of local public health emergency planning and response. You know, the best vaccine and surveillance in the world won't save any lives if there is no one at the local level to give the vaccine to the people.

Again, Mr. Chairman, I thank you for the opportunity to testify before you today. I would be pleased to answer any questions you may have.

[The prepared statement of Ms. Miller follows:]

NACo National Association of Counties

STATEMENT OF

THE HONORABLE KAREN MILLER

PRESIDENT
NATIONAL ASSOCIATION OF COUNTIES

COMMISSIONER
BOONE COUNTY, MISSOURI

LOCAL PREPAREDNESS: INFLUENZA AND MAJOR PUBLIC HEALTH THREATS
BEFORE THE HOUSE GOVERNMENT REFORM COMMITTEE

FEBRUARY 12, 2004

Mr. Chairman, my name is Karen Miller, County Commissioner from Boone County, Missouri. Boone County is a small county in largely rural Central Missouri which is home to the University of Missouri, located in the county seat of Columbia. I am here today, not only as a County Commissioner, but also as President of the National Association of Counties (NACo)*. I am honored to testify before you and the Committee on this important issue as I am well aware of your distinguished career in county government. I am also pleased to share the panel with others who recognize the importance of our nation's public health preparedness.

Additionally, I would especially like to thank the National Association of County and City Health Officials for their expertise in county public health issues and their assistance with my testimony today.

America's 3,066 counties vary in geographic shape, size, population, and in the services we provide, but one common thread is that we all play an integral role in protecting our communities. Counties are the nation's "first responders" who respond to virtually every emergency situation, whether it is a flood, an act of terrorism, or the outbreak of disease. This includes small rural counties, such as Boone County, which make up 2/3 (over 2100) of our nations counties.

Mr. Chairman, I have one overall message for you today: *We have made much progress in public health preparedness, but we have a long way to go.* At the local level, the people who work diligently on influenza immunization are the same people who are working every day to improve public health preparedness for any type of emergency. As the public health threats to which they must respond increase, we are asking the same people to do much, much more with resources that still are very limited. Today, on behalf of the nation's counties, I urge two actions: 1) Sustained and increased federal funding for public health preparedness; and 2) Greater, systematic attention by federal policy makers to the realities of local public health emergency planning and response.

*NACo is the only national organization representing county government in the United States. Through its membership, urban, suburban and rural counties join together to build effective, responsive county government. The goals of the organization are to: improve county government; serve as the national spokesman for county government; serve as a liaison between the nation's counties and other levels of government; achieve public understanding of the role of counties in the federal system.

As this Committee has recognized, our communities must be prepared for any disease outbreak, whether it results from an act of nature or an attack of terror. We have all been concerned about the potential for widespread influenza, because we have seen how it can take the lives of our children. We remember the scares caused by the anthrax attacks of 2001, and we want to be sure we know what our communities will do if the unthinkable occurs.

The good news is that the nation's counties are better prepared now than they were two years ago. The infusion of federal funds for building state and local public health capacities has helped a great deal. The plans that are in place will serve us well, whether we face an outbreak of influenza or smallpox.

We have already benefited from improved public health preparedness, even though there has been no truly catastrophic event. For instance, although we hope we will never see a case of smallpox, we have made great progress in planning for mass vaccination. Public health agencies know what they would have to do to mobilize and carry out vaccination of large numbers of people in a short time. Those same plans can be used, and have been used, in events where localities have had to address other public health emergencies. When we are prepared to mount a mass smallpox vaccination effort, we can also do the same for influenza.

In my own county, the work we did last year on developing a local health alert network, which was aided in part by public health preparedness grant funding, improved our response to influenza this year. It enabled us to share current local data about flu cases and state and CDC recommendations with our local medical providers. Our new grant-funded regional epidemiologist created weekly influenza summaries that we sent out to the medical community via the local health alert network. This has improved physician reporting of influenza, which is essential to help us identify any large outbreak. A regional public health information officer, also hired with public health preparedness grant funds, serves us and 16 other counties. This has enabled us to be more proactive in educating the general public about flu vaccination and how to prevent the spread of flu.

However, when my health department, or any local health department, needs to respond to influenza, or to a requirement to vaccinate medical personnel against smallpox, as we did last year, we are still using the same staff that carries out routine public health activities. The number of hours required to plan and carry out vaccination clinics pulls many people away from routine duties and those come to a halt. We just don't have the resources or staff to compensate for these demands. Of the approximately 3,000 public health departments in the country, nearly all are understaffed and under funded. Estimates suggest that more than 15,000 public health workers are needed nationwide. In Arlington County, Virginia for instance, it takes 90 people to set up one clinic for mass vaccination or mass distribution of medication.

What we want you to understand is that we have drawn upon far more local resources than federal funds to move forward in public health preparedness. The federal funding has brought important assistance to local health departments, such as more state laboratory capacity to identify disease agents quickly, and more support from epidemiologists. That is critical and we are grateful. However, the real work of preparing for and responding to public health emergencies locally takes place with the same people and facilities that we have always had. We are asking our public health nurses, educators, technicians and administrators to do a great deal more with less.

We still have a long way to go. We know that large-scale influenza or SARS might resurface in any community at any time. However, we have never had to implement large-scale isolation and quarantine. The logistical problems of doing this, and making sure that large populations remain safe and healthy, are quite overwhelming. Plans for these extreme, complex measures are not fully developed many places. We are plowing new ground.

In addition, many communities are concerned that they lack adequate arrangements for what we call "surge capacity," that is, extra doctors, nurses, epidemiologic investigators, and others who are not needed all the time, but would need to be called into service to contain an outbreak and care for patients in an emergency. Also, electronic information systems that are so necessary for communication and gathering data about the occurrence of diseases are improving, but there is still a very long way to go to achieve the seamless communication and interoperability that we need.

It is essential that the federal government remember that public health preparedness is not a destination that some day we will reach and then be able to stop. Rather, it is a journey during which we will improve little by little, day by day and year by year. We must always be using exercises to test our abilities and we must always be training new people, adapting to new technologies, and preparing to address new threats.

The influenza season is not quite over, but it is clear that, despite many tragic deaths, this was not the pandemic that we all fear. However, local public health departments were intensely occupied in addressing a pressing need to immunize as many people as possible and dealing with the sudden unavailability of vaccine. We have long experience in promoting and providing immunization and have dealt with vaccine shortages before. We think we did a good job under adverse circumstances.

Most local public health departments had plans for identifying stocks of available vaccine and reallocating vaccine among providers in their community. Many localities also tapped into their own funds to purchase vaccine for children and high-risk adults, when it was still available. State-based electronic reporting systems, such as the Health Alert Network funded with federal bioterrorism dollars, were used to report surpluses and shortages and help redistribute vaccine within states. To help prevent the spread of influenza, many localities launched public education campaigns with whatever resources they had available, using the mass media, posters, web sites, outreach to physicians and schools, to teach good hand hygiene and cough etiquette and the difference between a cold and the flu. The documents that CDC made available helped localities craft their own messages, but there is still a need for CDC to help us by crafting short, simple messages that we can use as they are, rather than having to boil down longer, more technical information ourselves.

The unexpected demand for flu vaccine and its subsequent unavailability concerned us because it required us to change our strategies and our public messages midstream. In prior years, local public health departments have promoted flu vaccination vigorously, particularly for high-risk groups such as the elderly. We know that it can save many lives. It pained us greatly when we found ourselves unable to offer vaccination to all who asked, particularly because the Flumist vaccine that remained available is unsuitable for children and the high-risk groups on whom we focus our service. There were approximately 70 counties in my state alone, who experienced a flu vaccine shortage this year and it is much too costly to overstock.

Public health requires good collaboration between federal, state and local governments, because each has an important, unique role to play. The fact remains, though, that disease outbreaks don't occur in states. They occur in communities and it is our counties and cities that bear the greatest burden for response. Local jurisdictions know better than the state what they need to be prepared. They know what their staffing needs are, what their training needs are, and how they could make the most efficient use of limited funding.

There are states in which many localities believe that they could be benefiting far more from federal bioterrorism preparedness dollars if the state were responsive to their needs and priorities. Moreover, we are deeply concerned that the Administration has proposed to cut the funding to CDC for upgrading state and local public health capacity by 11 percent. The local needs are compelling and they grow every day, as new health threats arise.

In addition, it is essential to understand that public health preparedness at the local level does not involve only public health departments. It is part of our overall emergency management system, with all its public and private partners. Across the nation, public health personnel are working closely with other local emergency management, fire and law enforcement personnel. Although public health professionals at the local, state and federal levels will provide leadership and expertise in a public health emergency, any community's success will depend on good communication and cooperation among all of our public safety agencies. There are a number of different federal funding streams for emergency readiness, but they all come together at the local level.

In closing, I'd like to re-emphasize the need for sustained and increased federal funding for public health preparedness and greater, systematic attention by federal policy makers to the realities of local public health emergency planning and response.

Again, Mr. Chairman, I thank you for the opportunity to testify before you today. I would be pleased to answer any questions you may have.

Chairman TOM DAVIS. All right.

Dr. Pien from Chiron. Thank you very much for being here.

Mr. PIEN. Thank you, Chairman Davis and Mr. Waxman, for the opportunity to appear today.

Drs. Gerberding and Fauci have provided the committee with an excellent characterization of this past flu season. I would just like to emphasize one point. Over 80 million Americans were vaccinated this past season, probably the highest ever. This is a significant public health milestone, for which the men and women working for public health should be recognized.

I would like to convey three key messages to this committee: one, Chiron is committed to meeting demand for flu vaccines in the United States; two, raising demand is key to increasing supply in both the normal and the pandemic flu seasons; and three, public-private partnerships are fundamental to increasing the country's preparedness for the normal and the pandemic flu seasons.

To my first point, our commitment. Chiron invested $878 million this past July to acquire the English company PowderJect, and the principal driver was the Fluviron and our flu vaccine business, of which 90 percent is in the United States. Over the last 4 years, we have tripled our capacity to 38 million doses for the U.S. market in 2003, and in 2004 Chiron plans to produce 50 million doses, a 30 percent increase over the prior year. We will shortly break ground on a $100 million new bulk manufacturing facility. Chiron is investing in bringing innovation to the U.S. market. This month we plan to file an IND application for our cell culture flu vaccine. Cell culture, as you heard, is viewed by many as one of the best ways to defend against a possible future pandemic.

To my second point, demand and supply being intertwined. Demand for vaccines drives increased supply and, therefore, steadily increasing demand in normal or interpandemic seasons is key to the preparedness for a pandemic. Put another way, reliable vaccine supply in a pandemic situation is dependent upon steadily increasing vaccine demand in the interpandemic seasons.

In the short-term, a government guarantee to create a strategic reserve may increase consistency of supply, but only if it does not undermine the current private sector distribution system and the public health distribution system at the different levels of the government and, more importantly, does not undermine the motivation of the private sector to invest in product and technology innovation. Public health interest is therefore best served by achieving the Healthy People 2010 goal of vaccinating 150 million people every year. This will reduce the need for the reserve over time.

And this brings me to my third point, the public-private partnership. Public-private partnership is key to raising demand and increasing pandemic preparedness. The Health and Human Services agencies must be fully funded to continue their leadership role in these activities. Strengthening our public health infrastructure to increase immunization rates in the interpandemic years is the single most important initiative today to prepare for tomorrow's pandemic.

To maximize the country's preparedness for a pandemic, Chiron believes that the Congress, the administration, and the private sector must work together on three things: one, expediting the already

existing scientific collaborations between the private sector and the scientists at the NIH to develop new vaccines; two, defining a pathway for speedy regulatory approval of a vaccine for the pandemic season; and three, clarifying the financing and the indemnification mechanisms now to ensure rapid initiation of production before the pandemic arrives.

A pandemic flu is a menacing threat to the Nation's health. Chiron pledges to be part of the solution. In the event of a pandemic, Chiron will cease production of our trivalent vaccine for the normal season and transition to a year-round production for a monovalent vaccine. Chiron will aim to triple the number of doses produced, subject to egg availability. Fifty percent of our output would be from our FDA licensed facility in Liverpool. Once Chiron's cell culture flu vaccine is approved, capacity will be expanded even further. Cell culture will eliminate egg supply as a bottleneck to speedy production.

My conclusions are therefore threefold: Chiron has invested heavily in the flu arena and in the public health interest of our Nation; Chiron is committed to bringing cutting-edge technologies to the United States to alleviate the threat of a pandemic over time; Chiron has been and shall continue to be part of the vibrant public-private partnership in vaccinology, which is essential to the Nation's long-term health.

On behalf of Chiron, thank you very much for the opportunity to express these views.

[The prepared statement of Mr. Pien follows:]

CHIRON

Statement Presented To

Committee on Government Reform

United States House of Representatives

By Howard Pien

President and CEO

Chiron Corporation

February 12, 2004

Introduction

Mr. Chairman, Members of the Committee: Thank you for the opportunity to provide a statement to the House Government Reform Committee at today's hearing. I am Howard Pien, president and CEO of Chiron Corporation, a global biotechnology company headquartered in Emeryville, California. Chiron Corporation, founded in California in 1981, is composed of three business units: BioPharmaceuticals, Blood Testing and Vaccines. Chiron is dedicated to research and innovation addressing global public health challenges. Through Chiron's breakthrough research discoveries in the fields of hepatitis B virus, human immunodeficiency virus and hepatitis C virus, millions of potentially fatal infections have been prevented.

Overview of Chiron

Chiron is the fifth-largest vaccines producer in the world, with sales of $678 million in 2003. Chiron Vaccines produces pediatric and adult vaccines to prevent life-threatening illnesses. These vaccines, which are sold throughout the world, have protected millions of people globally from *N. Meningitidis* Group C, polio, measles and other potentially fatal diseases. Chiron is a leading supplier of oral polio vaccine, producing more than 800 million doses annually to support global polio eradication efforts. Our rich heritage in vaccines is traced to the three European manufacturers Chiron has acquired over the past two decades, all of which were founded 100 years ago or more. The company has production facilities in Liverpool, United Kingdom; Siena, Italy; Marburg, Germany; and Ankleshwar, India; and it carries out research in Siena, Marburg and Emeryville. Chiron has a successful record of product development, including the launch of the first recombinant vaccine against pertussis, the first adjuvanted influenza vaccine and a conjugate vaccine against *N. Meningitidis* Group C.

Chiron currently has two vaccines licensed in the United States: Fluvirin® flu vaccine, one of only two injectable influenza vaccines approved by the U.S. Food and Drug Administration, and RabAvert® rabies vaccine, approved by the FDA in 1997. Chiron also supplies diphtheria and tetanus (DT) concentrate to GlaxoSmithKline for use in its DT-containing vaccines licensed by the FDA.[1] In addition, Chiron has initiated Phase III studies in the United States with the aim of licensing its conjugate vaccine against *N. Meningitidis* Group C, Menjugate®.[2]

Chiron and Influenza Vaccines

Chiron Corporation's $878 million acquisition of PowderJect Pharmaceuticals and its influenza vaccine Fluvirin in July 2003 represents a major commitment to ensuring that an adequate supply of vaccine is available to meet the needs of the United States. The principle driver for the acquisition was Fluvirin, which is produced at the company's FDA-approved and FDA-licensed facility in Liverpool. Approximately 90 percent of the production from the facility is delivered to the United States, with most of the remainder going to the United Kingdom.

Prior to its acquisition of PowderJect, Chiron was the third-largest producer of influenza vaccines globally and the second-largest supplier of influenza vaccine outside the United States. Today, Chiron is the second-largest producer of influenza

[1] Infanrix (DtaP) & Pediarix (DtaP-HepB-IPV)

[2] Menjugate® has been licensed in Europe via the Mutual Recognition Procedure and is also approved in other countries, including Canada and Australia.

vaccines in the world, with production of approximately 75 million doses annually. Chiron produces influenza vaccines at its facilities in Liverpool, Marburg and Siena and offers a number of influenza vaccines.

Currently, all influenza vaccines marketed in the United States are produced in embryonated hens' eggs from designated chicken flocks. Individual lots of each of the three virus strains are grown in the eggs and harvested. The harvested virus is inactivated (killed), purified and separated from the egg proteins, usually by high-speed ultra-centrifugation. The whole virus concentrates are then further purified and split (split vaccine) or purified, as for Fluvirin, such that the vaccine contains predominately only the hemagglutinin and neuraminidase virus coat proteins (surface antigen or sub-unit). The monovalent (single-strain) antigen lots are then sterile-filtered and Quality Control and potency tested. The monovalent lots are then formulated into trivalent vaccine (following FDA release), filled into the final containers and packed. The final run of primary antigen production in eggs is usually completed by September to allow time for processing, FDA potency assignment, vaccine formulation, packaging, QA release and shipping to have completed release of the product into the marketplace by October or November.

In addition to its conventional egg-based influenza vaccines, Chiron is pursuing development of a cell culture–based subunit influenza vaccine using the Madin-Darby Canine Kidney (MDCK) cell line. Chiron's influenza cell-culture research program has completed Phase II clinical trials, with licensure in Europe projected sometime during the latter half of the decade. A Chiron influenza cell-culture production facility for full-scale production of the vaccine exists in Marburg. Chiron has initiated discussions with the FDA and plans to submit an Investigational New Drug Application to pursue licensure of an influenza cell-culture vaccine in the United States.

While there do not appear to be significant clinical advantages to cell-culture vaccines as compared with the current egg-based vaccines in terms of safety and efficacy, the cell-culture production process offers several potential advantages. The overall process is more flexible and can be more easily adapted to increases in market demand. Additionally, the fermentation process is highly compliant with Good Manufacturing Practice (GMP) compliance.

In the event of an influenza pandemic, the cell-culture production process could offer significant benefits compared with the conventional process, including:

- Increased production capacity via faster initiation of continuous manufacture.
- Lack of dependence on a supply of eggs, which could be a key rate-limiting step in meeting an urgent public health crisis. Production can start at any time and can easily be expanded to full-year production.
- Reduction of production lead-time by six to eight weeks.
- Cell-culture production, unlike egg-based production, is a closed process that can be easily upgraded to Class III bio-safety standards that may be required for the management of a pandemic strain.
- Cell-culture production is suited to producing vaccines for influenza of avian origin, which will not grow on eggs without genetic modification.

Overview of Egg-Based Influenza Vaccine Production

Influenza vaccine usually contains three different influenza strains that are recommended by the World Health Organization (WHO) and FDA. The strains are selected to match the families of influenza viruses expected to be circulating each winter, following WHO continuous surveillance. The vaccine has a new composition each year, and the vaccine therefore cannot be stockpiled but must be made to order each year. In addition, influenza vaccine is a seasonal product, with the majority of immunizations occurring in the September-to-November time frame in the United States. If there is surplus vaccine that is unused at the end of the season, it cannot be reused the following year and must therefore be destroyed. The requirement for Southern Hemisphere influenza vaccine in the January to March season is comparatively small and usually of a different composition.

Vaccine manufacturers try to match annual supply and demand, ensuring enough doses are available to meet demand while avoiding wasteful destruction of unused vaccine at the end of the season. The inability to carry over inventory into the following season means that the margin of error is much smaller than for other vaccines. Forecasting demand accurately is complicated by the fact that it is not possible to assess the severity of the epidemic and then adjust production volumes; additional capacity cannot be added at short notice and must be planned at least one season in advance. The cycle time for vaccine production means that demand must be predicted based on historical data, without an indication of the severity of the current influenza epidemic.

Supply of Influenza Vaccine in Interpandemic Years

It is important to put the 2003 influenza season and the resulting demand for influenza vaccine into perspective by comparing it with previous years in which the influenza epidemic was less severe. In 2003, all supplies of injectable influenza vaccine produced for the United States appear to have been used, resulting in an estimated 83 million Americans being immunized against influenza. A milestone was reached: The estimated 83 million Americans immunized represent the highest immunization rate ever for influenza. Prior to 2003, immunization rates had remained relatively static, and unused vaccine had to be destroyed. For example, it is estimated that approximately 12 million doses were destroyed in 2002. It seems safe to assume, given the severity of the epidemic and the publicity in the media in 2003, that more people would have been immunized had additional supplies of influenza vaccine been available. Therefore, it is not surprising that the focus has been on the shortage of vaccine that occurred and how to prevent its occurrence in the future rather than the victory in reaching this public health milestone.

While one cannot underestimate the potential severity and impact of an influenza pandemic on the United States, ensuring an adequate supply of vaccine and achieving high immunization rates in interpandemic years is of major importance from a public health perspective. Influenza pandemics are irregular events occurring infrequently, approximately once every few decades. The influenza epidemic is an annual event, which was estimated during the 1990s to have caused an average of approximately 36,000 deaths per year[3] and 114,000 hospitalizations in the United States. This represents a significant burden of disease even when compared to the impact of a

[3] Source: Morbidity & Mortality Weekly Report 2003, Vol. 52 RR8

pandemic. It is estimated that approximately 500,000 deaths due to influenza occurred in the United States between September 1918 and April 1919 and that the pandemic caused 20 million deaths worldwide. The 1918–1919 pandemic was the worst pandemic recorded, and mortality in more recent pandemics has been lower. The Asian influenza pandemic of 1957 is estimated to have caused approximately seventy thousands deaths in the United States while the Hong Kong influenza pandemic of 1968 is estimated to have caused 33,000 deaths.[4] Therefore, while pandemic preparedness is crucial from a public health perspective, the public health benefits of implementing a routine influenza immunization program in interpandemic years should not be underestimated. Not only would it help prepare the United States in the event of a pandemic by ensuring that production capacity and mechanisms for distribution and delivery of vaccine are in place, but it also would reduce the annual burden of disease and death due to influenza.

The following must be in place in order to minimize the burden of disease caused by the annual influenza epidemic:

- An adequate supply of influenza vaccine in non-pandemic seasons to protect the population.
- Appropriate mechanisms to ensure delivery of the vaccine to the target populations.
- High public awareness on the need for immunization to ensure use of the vaccine by the target population.

Prior to its acquisition of PowderJect, Chiron was not committed to entering the U.S. influenza market for economic reasons. However, over the last few years, significant changes in the dynamics of the U.S. influenza market have occurred. The key changes are:

- The recommendations of the Advisory Committee on Immunization Practices (ACIP) on influenza immunization were broadened to include individuals between 50 and 64 years of age and healthy children between 6 and 23 months of age, significantly expanding the potential market for influenza vaccine.
- Pricing of influenza vaccines has reached a level that allows manufacturers to invest in maintaining facilities to meet FDA standards and in expanding manufacturing capacity in order to meet the increased demand.
- Reimbursement rates for providing influenza injections have been increased to levels at which physicians are encouraged to actively immunize patients.

These changes in market dynamics were key factors in Chiron's decision to acquire PowderJect and expand its strong presence in the influenza market to include the United States. There has been considerable comment in the media about the decision of three influenza vaccine manufacturers to discontinue production over the past few years and the resulting decrease in supply. However, it should be noted that two of the producers exited at a time when the market price of the vaccine was significantly lower, making it difficult to justify the investment required to maintain facilities to FDA standards or to consider an increase in capacity. The changes in market conditions over the past few years have resulted in a reduction in the barriers to investment, and the impact of these changes are beginning to be felt.

[4] Source: www.cdc.gov/od/nvpo/pandemics

The shift in dynamics has had a significant impact on investment decisions and capacity at Chiron. Over the past five years, investments of approximately $70 million in both primary (bulk) and secondary (fill/finish) manufacturing have been made to increase the production capacity of the Liverpool facility. This investment has resulted in a significant increase in the amount of Fluvirin supplied to the United States: The amount of Fluvirin supplied to the United States on an annual basis more than tripled from 12 million doses in 2000 to 38 million doses in 2003. Additional increases in production capacity and, consequently, to supply to the United States are planned for 2004 and beyond. Chiron is projecting that it will be able to produce approximately 50 million doses of Fluvirin in 2004, with the vast majority destined for the United States. If sufficient demand for influenza vaccine exists, Chiron plans to increase its production capacity and supply of influenza vaccine to the United States even further beyond 2004.

Building on recent investments to increase manufacturing capacity at the Liverpool facility, Chiron is committing an additional $100 million dollars to replace the existing influenza bulk manufacturing facility in Liverpool with a new "state of the art" facility[5] to complement the secondary manufacturing facility opened in 1998. This commitment is being made to ensure that Chiron is in a position to continue to supply Fluvirin to the United States and to add incremental capacity until the FDA approves its cell-culture vaccine and sufficient cell-culture production capacity is available to meet the market needs in the United States.

It should be recognized that changes in market dynamics, specifically the increase in price that has occurred over the past three years, have reversed the trend of decreasing manufacturing capacity as producers are investing in capacity increases and upgrading facilities and licensing cutting-edge technologies for the U.S. market. Chiron manufacturing investments are not unique to the industry, suggesting that the growing U.S. influenza market is an important public health priority that the private sector must ensure is met. However, given the nature of biologics manufacturing there is inevitably a lag between the decision to invest and improved capacity as a result of that investment. The United States is only now beginning to see the impact of the positive changes in market dynamics that occurred a few years ago with regard to expanded investment in manufacturing capacity.

The early onset of the 2003 influenza season and the resultant increase in demand above levels seen in previous influenza epidemics created a shortage of vaccine which has led to concerns in the media and general population about the fragility of influenza vaccine supply and its potential impact on the health of the U.S. population. However, the influenza vaccine supply situation is much less fragile than for many other commonly used vaccines in the United States. The recent Institute of Medicine Report "Financing of Vaccines in the 21st Century Assuring Access and Availability"[6] highlighted the fact that a single source of supply existed for six of the recommended vaccines[7] in the United States. This means that no backup capacity is available should a manufacturer experience production problems or other disruptions creating a

[5] A new fill/finish facility was completed a few years ago.
[6] Institute of Medicine, August 2003
[7] Tetanus-diphtheria, measles-mumps-rubella, varicella (chicken pox), pneumococcal conjugate, meningococcal polysaccharide, pneumococcal polysaccharide

significant potential for supply interruptions. Indeed, these have occurred over the past few years. In 2001 and 2002, eight of the 11 recommended childhood vaccines were in short supply.[8] These shortages impacted immunization policy in the United States, forcing the ACIP to temporarily revise its recommendations on pneumococcal conjugate vaccine and diphtheria, tetanus and pertussis (DtaP) and to recommend that varicella (chicken pox) immunization be pushed back to 18-24 months from 12-18 months. In contrast, there are now three sources of supply for influenza vaccine, making a complete disruption of supply an unlikely event.

Key public policies are of critical importance to ensure that influenza production in interpandemic years is adequate. A competitive environment that encourages multiple suppliers of vaccines to ensure continuity of supply is vital. Implementation of any public purchase program with a "winner take all" approach could have the unintended impact of discouraging potential suppliers by increasing the risk associated with participating in the market, as production is impossible to plan in an "all or nothing" situation.

The shortage of vaccine in 2003 has led to a tremendous focus on the supply side of the equation and mechanisms for increasing supply to meet an above-ordinary level of demand. A key lesson learned was that demand for influenza vaccine in a severe epidemic can reach levels above those anticipated for a more typical season and that producers are not able to adjust supply to meet the surge in demand once the season has started. The production cycle times for influenza vaccine are such that by the time the surge is identified it is too late to increase supply to meet the increase in demand. This has led to proposals aimed at ensuring a sufficient supply of influenza vaccine for the United States in the event a severe epidemic leads to a surge in demand. Many of the proposals involve mechanisms guaranteeing purchase of influenza vaccine by the federal government with a primary objective of creating a strategic reserve to meet an above-average level of demand for influenza vaccine. Essentially, the purpose of these purchases would be to provide insurance against a severe epidemic by encouraging manufacturers to expand capacity to produce volumes above predicted levels of demand in the event of a typical epidemic. The premise of the mechanism would be to transfer the risk of investing and carrying excess inventory from the producers to the federal government.

As Congress and the Administration consider these proposals, Chiron is committed to working collaboratively with you to craft balanced solutions. Together we must fully consider issues relative to the timing of implementing new approaches to supply, opportunities to expand immunization rates to meet the Healthy People 2010 objectives, and the potential risk to existing supply and distribution channels. Chiron's perspective is as follows:

- Chiron is prepared to increase its supply of influenza vaccine by extending the production season and delivering additional doses in late November and December. At present, Chiron does not do this, as U.S. demand for influenza vaccine after November does not usually occur. Based upon U.S. immunization trends prior to 2003, extension of the production season heretofore would have led to unused vaccine that would have ultimately been destroyed.

[8] USA Today, February 18, 2002

- The go/no-go decision on whether to extend the production season needs to be made early in the year to guarantee the supply of eggs required for vaccine production. Therefore, a commitment to purchase the doses would need to be made prior to this date, when no real indication of the severity of the epidemic exists. Theoretically, a go/no-go decision on extending the production season could be made in June. However, a concern exists regarding reliability of egg supply, and this would not be the optimal solution on an ongoing basis.
- In order to maximize the benefit of the program, guaranteed purchase of vaccine should be distributed among all suppliers who are able to provide vaccine.
- Demand created by these purchases would be artificial if not accompanied by an increase in vaccinations, as the incremental doses would be destroyed at the end of the season. While the primary intention of these purchases is to create a buffer to meet unanticipated surges in demand, concerns exist about the long-term viability of any purchase program where doses would be destroyed. Essentially, the program would achieve its goals in the short term, but Chiron believes that real demand for influenza vaccine must be increased if supply is to grow in the long term.
- Any expansion of government programs for the purchase influenza vaccine beyond existing programs, such as Vaccines for Children and 317 funds, should contain components to ensure expanded use of the vaccine in order to prevent destruction of unused doses at the end of the season, which could detrimentally impact the demand side of the equation.
- Government involvement, while it may be appropriate and necessary, may have unintended consequences that we need to be cognizant of and manage prospectively. Large-scale government purchases of vaccine have the potential of disrupting the current private-sector distribution system for influenza vaccines.

We believe that the factors highlighted above can be effectively managed in a prospective fashion by collaboratively developing a program to secure a strategic reserve by the government that does not create the unintended consequences or detrimentally impact the private market.

Ensuring increasing year-on-year demand for influenza vaccine under routine circumstances creates a market-efficient solution to the issue of meeting episodic surges in demand, as it prospectively balances supply and demand in the event of a severe epidemic. Furthermore, focusing on solutions impacting the demand side of the equation is important in the context of planned increased production capacity for future seasons. If demand remains static or returns to levels seen in 2002, a situation will exist where demand exceeds supply. As mentioned previously, 2003 represented the highest number of people ever immunized, and there is no guarantee that the same levels will be achieved in the event of a less severe epidemic.

Chiron's concern is that in future, if demand remains static, the United States will return to a situation where supply will again exceed demand, leading to unused vaccine doses being destroyed, as has occurred in the past. This would trigger a reassessment by Chiron of the need to increase influenza supply and, depending on any demand shortfall, may even lead to a reduction in supply in future years. We

should therefore not be complacent and assume that because excess demand existed in 2003, it will automatically spill over to future years and absorb projected supply for the U.S. market.

In order to raise influenza immunization coverage rates to effectively use the additional supply that will be available next year, key stakeholders (manufacturers, distributors, the public health community, providers and insurers) should collaborate on the following issues:

- Raising awareness of the immunization recommendations among the medical community and general population.
- Encouraging immunization by highlighting the benefits of immunization and developing innovative programs for facilitating access to the vaccine.
- Extending the immunization season into December to ensure all doses are used and to potentially increase the window in which vaccine could be supplied to the market.
- Creating an environment that supports manufacturers who produce doses at risk.

Furthermore, these efforts must not be limited to the 2004 season but must be continued for the long term. A significant increase in demand for influenza vaccine is required to achieve the Healthy People 2010 goals of 90 percent coverage rates of non-institutionalized adults 65 years of age and older and 60 percent coverage rates of high-risk non-institutionalized adults 18-64 years of age.[9] While these goals are ambitious, they are achievable if both the public and private sector collaborate on achieving them. The success of such partnerships in raising immunization rates for pediatric vaccines demonstrates how this approach can achieve positive results. It is recognized that there are differences between influenza vaccination and the pediatric immunization situation, where school entry mandates played an important role in raising coverage rates. Nevertheless, it is felt that some of the lessons learned would be applicable.

In conclusion, Chiron believes the building blocks are in place to ensure a reliable supply of influenza vaccine for the United States in interpandemic years because:

- The pricing environment has reached levels where it supports manufacturers' investment in production capacity for the United States, as evidenced by the investments made by Chiron and other producers in recent years. The results of these investments are beginning to be realized.
- Federal recommendations expanding significantly the number of individuals eligible for the vaccine are in place and production capacity is being increased to meet these targets.

Chiron believes that the main challenge moving forward will be ensuring that demand continues for the capacity that it projects will come on stream over the next few years. Based on the success of initiatives in raising pediatric immunization rates, it is believed that partnerships between key immunization stakeholders in the private and public sector represent the best option for increasing demand. Chiron wishes to partner with stakeholders and is prepared to invest resources in efforts aimed at

[9] The target rate for institutionalized adults aged 18 and older is 90 percent.

increasing immunization coverage. Finally, while Chiron believes guaranteed purchase of influenza vaccine by the federal government could provide a short-term solution to meeting above average demand in the event of a severe epidemic, provided incentives are properly structured, it is concerned about the long-term viability of any program that would artificially raise demand and result in surplus doses of vaccine being destroyed. Chiron therefore believes that focusing on increasing demand on an annual basis, thereby reducing the level of unexpected demand in the event of a severe epidemic, might provide a more viable long-term alternative. Chiron welcomes the opportunity to provide input into proposals as they are being developed.

As stated in a recent editorial in the New England Journal of Medicine:

> "Ultimately the experience of 2003-2004 may help us deal with influenza epidemics more effectively. The public awareness and media attention that accompanied reports of severe illness in children have resulted in greater recognition of both the severity of influenza in all age groups and the benefits of influenza vaccine. This recognition may spur increased use of vaccination and help us achieve the goals for vaccine coverage encompassed by the Healthy People 2010 Initiative. Increased demand for vaccine will encourage manufacturers to continue producing it, possibly in greater quantities. Increased production is critical toward developing the surge capacity that will be needed to deal with new pandemic viruses when they occur."[10]

U.S. Influenza Supply in a Pandemic

The impact of an influenza pandemic would not be limited to the United States, as the entire global population of 6 billion people would be at risk. The global nature of a pandemic presents a significant challenge to the public health infrastructure and to influenza vaccine manufacturers in particular. Chiron is committed to supporting pandemic preparedness efforts and is actively involved in pandemic preparedness working groups at both the international and national level:

- At the international level, Chiron co-sponsors a specialized group of influenza vaccine manufacturers, the Influenza Vaccine Supply Task Force (IVS TF), created in 2001 with the endorsement of the International Federation of Pharmaceutical Manufacturers Associations. The group is made up of 11 companies representing 80 percent of total global influenza vaccine production capacity. The IVS TF is providing industry input on pandemic preparedness planning to bodies such as the WHO, European Commission, European Medicines Evaluation Agency (EMEA), and other international, national and local health authorities.
- At the European level, Chiron, together with other influenza vaccine manufacturers represented by the European Vaccine Manufacturers (EVM) group, is directly involved in many activities regarding pandemic preparedness in Europe.
- Chiron submitted a pandemic capability statement in June 2003 at the request of the U.S. Centers for Disease Control and Prevention (CDC) and the National Vaccine Program Office (NVPO).

[10] Treanor, J., New England Journal of Medicine, January 15, 2004.

From the perspective of an influenza vaccine producer, planning for a pandemic represents a significant challenge due to the nature of the product being manufactured. Essentially, the following factors limit the ability to rapidly expand supply in the face of a pandemic under current circumstances:

- **Production capacity**—Influenza vaccine production capacity is aligned with annual demand for vaccine under normal circumstances, i.e., between pandemics, and therefore little or no surge capacity exists to meet pandemic demand.
- **Inability to stockpile**—Stockpiling of vaccine in preparation for a pandemic is not a viable strategy, as it is not possible to predict the vaccine strain that will cause the pandemic.
- **Supply of primary production material**—Currently, vaccines are produced using eggs, and ensuring an adequate supply of eggs to significantly increase production during a pandemic represents a significant challenge.
- **Specialized production facilities**—Additional quantities of vaccine could not be readily produced in facilities used for other vaccines, as production and purification equipment and facilities are specifically designed for influenza vaccines.

Chiron has plans to maximize production of influenza vaccine at its Liverpool, Marburg and Siena facilities to help overcome these challenges in the event of a pandemic. The following steps would be undertaken to increase vaccine production:

- **Year-round production**—Influenza vaccine production would be run continuously over the whole year as opposed to the current seasonal production cycle. However, it should be noted that this assumes that additional egg supply will be available to keep the facilities running year round.
- **Monovalent vaccine**—A monovalent vaccine containing the pandemic strain only would be produced as opposed to the standard trivalent vaccine containing three strains. Manufacturing capacity would therefore be increased by a factor of three, assuming that the vaccine contains the same amount of antigen as the conventional influenza vaccine.[11] Any increase in the antigen content of the pandemic vaccine would result in a proportional reduction in the number of doses that could be produced. At present, the clinical data available to support the definition of the pandemic vaccine is limited.

Chiron estimates that implementing these two steps in the event of a pandemic would more than triple its influenza vaccine manufacturing capacity, of which 50 percent would be produced at its FDA-licensed facility in Liverpool, assuming the pandemic vaccine contains the same amount of antigen as the normal vaccine. By the end of the decade, under its current plan, Chiron anticipates being able to increase its pandemic vaccine production by an additional 50 percent due to expanded production capacity in Liverpool and the availability of a cell-culture facility in Marburg producing its MDCK–based cell-culture vaccine.

[11] It should be noted that studies of experimental vaccines produced in response to the avian influenza A outbreaks in Hong Kong suggest that a greater dosage or an adjuvanted vaccine may be required. Therefore, whether this assumption will turn out to be valid is open to question.

Adjuvantation[12] of the pandemic vaccine could theoretically expand production capacity even further by reducing the required antigen dose. However, limited clinical data for the pandemic strain situation exist. Chiron therefore believes that it would be of significant benefit if publicly funded studies were undertaken with a goal of defining the characteristics (e.g., antigen and/or adjuvant dose) of a "pandemic-like" vaccine and vaccination schedule.

A pandemic would not represent a "business-as-usual" situation for Chiron. Implementing these steps to increase influenza vaccine production would occur at a cost of using resources normally devoted to the production of other vaccines. For example, producing the additional influenza vaccine would take up additional filling capacity impacting the ability to fill other vaccines. Therefore, production of the pandemic vaccine would potentially disrupt Chiron's ability to supply other vaccines to its customers. This disruption in supply could lead to public health consequences if alternative sources of supply could not be found or adequate stockpiles were not in place. At present, the impact of disruption of supply on the United States would be limited, as the only Chiron vaccine that could be impacted is its rabies vaccine. However, global markets for Chiron's pediatric and adult vaccines would be detrimentally impacted.

In the face of a potential influenza pandemic, switching production to a monovalent pandemic vaccine imposes a significant financial risk: If the predicted pandemic failed to materialize, there would be no demand for the monovalent vaccine, and Chiron would be forced to destroy the vaccine. Therefore, Chiron would be unlikely to make the decision to switch production from trivalent vaccine to a monovalent pandemic strain without a guarantee that its production would be purchased whether or not the pandemic materialized. Chiron would be unable to assume this risk without financial guarantees being in place due to the severe consequences of losing an entire year's revenues generated from the production of influenza vaccine. Therefore, in order to trigger a switch to pandemic vaccine production as quickly as possible in the event of a potential pandemic, governmental guarantees to purchase the vaccine and an agreed-upon purchase mechanism should be in place. The need for a mechanism to guarantee purchase implies a limited role for the private sector in the marketing of a vaccine in the event of a pandemic. National governments will procure the vaccine, be responsible for its distribution and determine the priority of immunization. Based on these considerations, Chiron assumes that in the event of a pandemic, the market for influenza vaccine will be almost exclusively a public-sector market, with national governments purchasing vaccine from producers. In addition, Chiron assumes a mechanism for indemnifying manufacturers, similar to that of smallpox, will be in place.

It is important to note that the current regulatory approval process would have to be expedited in order for manufacturers to rapidly convert to producing a monovalent pandemic vaccine in a timely fashion. Under the present system, obtaining regulatory approval could be a bottleneck in supplying pandemic vaccine. Chiron believes that discussions and planning should occur now between manufacturers and the FDA in

[12] Adding an adjuvant, a substance that improves the immune response to the vaccine.

order to determine the regulatory pathway for approval of a vaccine, including any amendments to official release requirements in the event of a pandemic. This would be of significant value to expedite the availability of supply should the pandemic occur.

Despite a potential increase in the supply of vaccine by a factor of greater than three, there will be a global shortage of influenza vaccine in the event of a pandemic. Demand for influenza vaccine would increase dramatically compared to normal circumstances due to the need to immunize most of the global population and a potential increase in the number of doses required per person to provide immune protection from one to two. Current global influenza vaccine production capacity, estimated at roughly 300 million doses in a typical year,[13] will most likely be unable to cope with global demand, and therefore a shortage of vaccine is expected to occur.

Chiron is committed to maintaining supply to the United States in the event of a pandemic. However the current location of Chiron's influenza manufacturing facilities outside of the United States imposes constraints on its ability to ensure this occurs, as it is not clear how global allocation of the vaccine will take place in the event of a pandemic. Where demand outstrips supply, it is possible that national authorities will impose constraints on the allocation of influenza vaccine by manufacturers under their jurisdiction. One of the constraints that may be imposed by national authorities is that producers be required to give priority to meeting national demand before shipping vaccine supply to traditional markets. For example, Chiron could be asked to give precedence to the United Kingdom in allocating vaccine supply from its Liverpool facility, as it is the only domestic source of supply for that country. Furthermore, once the needs of the United Kingdom were met, priority might be given to other European countries before allowing vaccine to be made available to the rest of the world. In addition, manufacturers with facilities located in European Union countries may be required by their national authorities to give precedence to the needs of other EU member countries once domestic needs have been met before vaccine can be exported outside of the EU, particularly for those member states that do no not have domestic production capacity. These variables are real and uncharted.

A critical success factor to pandemic preparedness efforts in the United States would therefore be increasing domestic production capacity of influenza vaccine in order to ensure a supply of vaccine free from external pressure in a pandemic. Ideally, this would involve creating new facilities rather than expanding capacity at the only domestic facility because, as stated previously, reliance on a single supplier is inherently risky.

If new facilities were to be built in the United States with a primary objective of ensuring supply of vaccine in the event of a pandemic they should be based on cell-culture technology as opposed to the current egg-based production. Cell-culture technology offers significant advantages in the event of a pandemic as previously highlighted in this statement. The private sector appears to represent the best option for expediting the availability of domestic cell-culture production capacity as access to a scaled-up production process would considerably shorten development timelines.

[13] Chiron internal estimate.

Chiron has yet to decide whether it will expand its planned cell-culture production capacity in Marburg in order to supply the U.S. market, but several potential scenarios for capacity expansion have been evaluated. These involve either increasing production at the Marburg site or developing a "green field" site in Europe, the United States or elsewhere for the production of influenza cell-culture vaccine. The decision as to which approach to take will primarily be based on financial considerations, such as the required level of capital investment and Chiron's ability to expeditiously commercialize influenza cell culture. A preliminary analysis suggests that capacity expansion at Marburg could be the fastest and probably most cost-effective option for Chiron due to the benefits of economies of scale in concentrating production at a single site. Developing a new facility on a "green field" site capable of producing 50-70 million doses of conventional trivalent influenza cell-culture vaccine and more than 200 million doses of monovalent pandemic vaccine is estimated to require a capital investment or more than $200 million.

To expedite pandemic preparedness, Chiron believes that the United States should consider providing incentives, such as tax relief or a contract to guarantee purchase of a certain volume of vaccine at a specified rate, to encourage influenza vaccine producers to locate cell-culture production facilities in the United States. The objective of these incentives would be to ensure that in a pandemic situation the United States has access to cell-culture influenza vaccine free from external government jurisdiction. These incentives should be structured to result in more than one production facility being developed so as to avoid reliance on a single supplier. Incentives should be structured to encourage the location of "bricks and mortar" in the United States as opposed to encouraging the development of a cell-culture vaccine. Financing the development of a vaccine may expedite licensure of a new product or products but would not guarantee that the source of supply will be located in the United States, a key objective for pandemic preparedness. Chiron believes that the private sector is best placed to rapidly bring these facilities on stream as vaccine producers have access to scaled up cell-culture manufacturing processes from production facilities located outside of the United States, which could easily be transferred to a new plant.

In conclusion, an influenza pandemic will represent a significant challenge to Chiron, as it will need to rapidly expand influenza vaccine at the expense of other products in its portfolio. Recognizing this challenge, Chiron is committed to supporting global pandemic preparedness efforts prior to the inevitable occurrence of a pandemic. Chiron believes that continuing to forge partnerships between vaccine manufacturers and the public health authorities is crucial in order to discuss and resolve the following issues:

- Increasing demand during interpandemic years to encourage increased capacity.
- Determining whether or not pandemic vaccine supply can be expanded by adjuvantation of the vaccine.
- Identifying the regulatory pathway for approval of a pandemic vaccine, including any amendments to official release requirements in the event of a pandemic.
- Establishing a mechanism to indemnify influenza manufacturers.

- Implementing mechanisms to trigger the switch to production of a monovalent pandemic vaccine through guarantees to purchase output whether or not the pandemic materializes.
- Incentivizing U.S. influenza manufacturing capacity.

In summary, Chiron has invested heavily in ensuring that the United States has a supply of influenza vaccine in interpandemic years. Chiron is committed to providing leadership in the U.S. influenza market. Chiron is shouldering the necessary risks to expand its ability to increase supply and is bringing cutting-edge technologies in influenza cell-culture production to the U.S. market. Fundamental to Chiron's success in realizing its commitments is the ability to work collaboratively with Congress, the Administration and public health officials to reach the immunization rates established in Healthy People 2010 while incentivizing the private sector to transition to new technologies in influenza immunization. These priorities are of critical importance if we are to effectively position the United States for preparedness for a global influenza pandemic.

Thank you for the opportunity to present the views of Chiron Corporation. I am happy to answer any questions you may have for me.

Chairman TOM DAVIS. Dr. Pien, thank you very much.

Dr. Young.

Dr. YOUNG. I am really happy to address the committee.

Chairman TOM DAVIS. Well, we are happy to hear you.

Dr. YOUNG. As you know, I am president of research and development at MedImmune, which is a biotech company located just north of here in Gaithersburg, MD. Today's topic is of particular interest to me, not only because of my relationship with MedImmune, but because I am actually a flu virologist by training.

As you may know, MedImmune manufacturers the new intranasal flu vaccine FluMist, which was licensed by the FDA in June 2003. FluMist, in addition to being the first intranasal influenza vaccine available in the United States, is a live attenuated vaccine that provides immunity both systemically, throughout the body, as well as in the nasal passages, where the virus actually enters the body.

Today I would like to share with you our opinion on what the most recent flu season has taught us about the United States' ability to protect its citizens against flu and, most importantly, about the country's ability to be prepared in a pandemic situation. Our thoughts are based upon our experience with FluMist in its first year of commercial availability.

After 30 years of development, costing approximately $1 billion, and three FDA Advisory Committee meetings, FluMist was finally licensed for the very limited population of healthy individuals aged 5 to 49 years. Because FluMist licensure occurred late in the influenza manufacturing cycle, we planned for a limited launch and manufactured at risk about a quarter of our total production capacity of 20 million doses of vaccine. Our manufacturing for the current influenza virus season was virtually flawless, making approximately 5 million doses of FluMist available to the consumer as early as September, well ahead of this year's early influenza season. Of these 5 million doses, about 65,000 doses were donated by our business partner, Wyeth, to college campus vaccination programs. Further, up to 3 million doses were made available for purchase by CDC at a discounted price of $20 a dose, a price at which, I might add, would require us to sell more than 8 million doses just to break even financially.

Unfortunately, close to 4 million of the 5 million doses remain unused to date, and will be destroyed at the end of this year's influenza season. Thus, in spite of MedImmune's best efforts to work proactively and cooperatively with public health authorities to bring to the market the first innovation in influenza prevention in more than 50 years, there were 4 million lost vaccination opportunities in this year's influenza season, which hit early and hard, and challenged the U.S. vaccine supply and distribution systems.

As such, as we analyze our initial "very disappointing" experience as a flu manufacturer, one of the options we are considering is whether we should remain in the vaccine business or whether we should "cut our losses and get out now" rather than face the overwhelmingly difficult regulatory landscape of bringing new and more effective vaccines to the marketplace. On our part, to simply achieve parity with the approved labeling of the old-line, inactivated vaccines, we must spend at least an additional $200 million

to achieve safety and efficacy standards the other vaccines were never required to achieve, or have ever independently proven for that matter. This double standard is more than enough reason to cause new manufacturers pause before entering the vaccine business, and our very public experience this season will most certainly have a chilling effect on others who are considering entry into this business.

What were some of the factors that contributed to the lost opportunities for vaccination? First, demand for the influenza vaccine is strongly influenced by policies set by the Federal health authorities. Currently, influenza vaccine recommendations primarily target persons who are less than 2 years of age or more than 50 years of age, or who have underlying medical conditions that put them at high risk for complications due to flu. However, the burden of influenza illness is significant in healthy persons who fall outside these targeted age groups, and in otherwise healthy unvaccinated school-age children who serve as vectors for transmission of the influenza to their families and to high-risk individuals with whom they are in contact. In fact, if you look at the flu season thus far, from October 2003 through February 2004, 121 influenza-associated deaths among children less than 18 years of age were reported by the CDC; 49, or 40 percent, were 5 to 17 years of age, and 95 of the children, or 79 percent, had no underlying medical conditions.

Therefore, MedImmune believes that the existing narrowly targeted influenza vaccine recommendations are woefully inadequate and must be expanded, and that influenza vaccine should be universally recommended for all Americans. This would further the objectives of influenza prevention, ensure continued development of new, innovative vaccines, and ensure availability of adequate supplies for annual and pandemic influenza seasons. Specifically, a universal recommendation would drive the demand for routine annual vaccination, which in turn will provide the impetus on the part of vaccine manufacturers to increase their production capacity to meet routine demand. This increased capacity will enable manufacturers to better respond to influenza not only on an annual basis but also in the event of a pandemic which would severely challenge existing vaccine capacity and the vaccine delivery infrastructure.

Recommendations by the public health authorities are necessary, but not sufficient, to ensure adequate vaccination of the American public. Federal authorities need to make the public aware of the significant burden of influenza in all populations, both healthy and high-risk, and must enthusiastically endorse new, innovative vaccines as they become licensed and available.

Another factor that contributed to lost opportunities for vaccination in the current influenza season was the misperception that FluMist could cause influenza, rather than prevent it, as it had just been approved by the FDA to do so, driven in part by erroneous information provided by public health authorities in public statements and on government Web sites that clearly stated, "that FluMist can cause the flu." While the statement on the Web site was ultimately changed, it was not changed until after the media ran with the erroneous information. These statements created damaging misperceptions of FluMist and its benefits, and most cer-

tainly reduced the number of people protected against this year's flu epidemic that included the virulent mismatched Fujian strain. "Accurate" educational materials from our public health officials are paramount to successfully sharing the benefits of vaccination to the general public and achieving broad immunization against the flu.

How is MedImmune contributing to the efforts to prepare for a pandemic threat? First and foremost, we have already made a considerable investment, to the tune of $1 billion, to overcome the extraordinarily high regulatory hurdles facing new vaccines in order to make available an important new option for flu vaccination. Second, should we ultimately choose to remain in the flu vaccine manufacturing business, we will undertake the financial burden of spending hundreds of millions of additional dollars to hopefully expand our indication to include persons younger than 5 and older than 49 years which, if we succeed in doing, will in turn hopefully increase the demand for FluMist that will then justify increasing our manufacturing output to full capacity. Third, we are working proactively with Federal authorities to develop and test a FluMist vaccine for use in a pandemic situation. And, fourth, we have worked closely with the World Health Organization to make MedImmune's intellectual property in the area of reverse genetic engineering available for development and testing of inactivated pandemic vaccines.

So in conclusion, the core of my message to you today is that in 2004, in the wealthiest and most powerful country on Earth with the world's best health care system, it should be unacceptable to all of us that more than 100 American children and countless elderly have recently died from a completely preventable disease. Importantly, this year is not unique. Every year 36,000 Americans die from influenza. The best way for us to be prepared to prevent this from happening in the future, as well as to help make sure we are prepared to deal with a pandemic situation, is to have the current flu vaccination recommendations expanded to include all Americans, especially expanded to include that all healthy children be vaccinated against the flu.

Thank you very much for the opportunity to present today.

[The prepared statement of Dr. Young follows:]

MedImmune, Inc.

MedImmune Oral Testimony
Congressional Hearing on Government Reform

By Dr. Jim Young
President of Research and Development

February 12, 2004

MedImmune Oral Testimony
Congressional Hearing on Government Reform, February 12, 2004

Good morning. My name is Dr. Jim Young, and I am the President of Research and Development at MedImmune, Inc, a biotechnology company headquartered in Gaithersburg, MD. Today's topic is of particular interest to me, not only because of my association with MedImmune, but also because I happen to be a flu virologist by scientific training. As you may know, MedImmune manufactures the new intranasal influenza vaccine, FluMist, which was licensed by the FDA in June 2003. FluMist, in addition to being the first intranasal influenza vaccine available in the U.S., is a live attenuated vaccine that provides immunity both systemically and in the nasal passages – the usual point of entry for influenza virus. Today I would like to share with you our opinion on what the most recent flu season has taught us about the United States' ability to protect its citizens against the flu and, most importantly, about the country's ability to be prepared in a pandemic situation. Our thoughts are based upon our experience with FluMist in its first year of commercial availability.

After 30 years of development, costing approximately $1 billion, and three FDA Advisory Committee meetings, FluMist was finally licensed for the very limited population of healthy individuals age 5 to 49 years. Because FluMist licensure occurred late in the influenza manufacturing cycle, we planned for a limited launch and manufactured at risk about a quarter of our total production capacity of 20 million doses of vaccine. Our manufacturing for the current influenza season was virtually flawless, making approximately 5 million doses of FluMist available to the consumer as early as September, well ahead of this year's early influenza season. Of these 5 million doses, about 65,000 doses were donated by our business partner Wyeth to college campus vaccination programs. Further, up to 3 million doses were made available for purchase by CDC at the discounted price of $20 a dose - a price at which, I might add, would require us to sell more than 8 million doses just to break even financially. Unfortunately,

close to 4 million of the 5 million doses made remain unused to date, and will be destroyed at the end of this year's influenza season. Thus, in spite of MedImmune's best efforts to work proactively and cooperatively with public health authorities to bring to market the first innovation in influenza prevention in more than 50 years, there were 4 million lost vaccination opportunities in this year's influenza season, which hit early and hard, and challenged the U.S. vaccine supply and distribution systems. As such, as we analyze our initial "very disappointing" experience as a flu manufacturer, one of the options we are considering is whether we should remain in the vaccines business, or whether we should "cut our losses and get out now" rather than face the overwhelmingly difficult regulatory landscape of bringing new and more effective vaccines to market. On our part, to simply achieve parity with the approved labeling of the old-line, inactivated vaccines, we must spend at least an additional $200 million to achieve safety and efficacy standards the other vaccines were never required to achieve (or have ever independently proven for that matter). This double standard is more than enough reason to cause new manufacturers pause before entering the vaccine business, and our very public experience this flu season will most certainly have a chilling effect on others who are considering entry into the business.

What were some of the factors that contributed to the lost opportunities for vaccination? First, demand for influenza vaccine is strongly influenced by policies set by federal health authorities. Current influenza vaccine recommendations primarily target persons who are less than 2 years of age, more than 50 years of age, or who have underlying medical conditions that put them at high-risk for complications due to influenza. However, the burden of influenza illness is significant in healthy persons who fall outside these targeted age groups, and in otherwise healthy unvaccinated school-age children who serve as vectors for transmission of influenza to their families and to high-risk

individuals with whom they are in contact. In fact, if you look at the flu season thus far from October 2003 through February 3, 2004, 121 influenza-associated deaths among children less than 18 years of age had been reported to CDC. Forty-nine of the children (or 40%) were 5 to 17 years of age, and 95 of the children (or 79%) had no underlying medical conditions. Therefore, MedImmune believes that the existing narrowly targeted influenza vaccine recommendations are woefully inadequate and must be expanded, and that influenza vaccine should be universally recommended for all Americans. This would further the objectives of influenza prevention, ensure continued development of new innovative vaccines, and ensure availability of adequate vaccine supplies for annual and pandemic influenza seasons. Specifically, a universal recommendation will drive the demand for routine annual vaccination, which will in turn provide the impetus on the part of vaccine manufacturers to increase their production capacity to meet routine demand. This increased capacity will enable manufacturers to better respond to influenza not only on an annual basis, but also in the event of a pandemic, which would severely challenge existing vaccine capacity and the vaccine delivery infrastructure. Recommendations by public health authorities are necessary, but not sufficient to ensure adequate vaccination of the American public -- federal authorities need to make the public aware of the significant burden of influenza in all populations (both healthy and high-risk), and must enthusiastically endorse new innovative vaccines as they become licensed and available.

Another factor that contributed to lost opportunities for vaccination in the current influenza season was the misperception that FluMist would CAUSE the flu rather than prevent it as it had just been approved by the FDA to do - driven in part by erroneous information provided by public health authorities in public statements and on government web sites that clearly stated "that FluMist can cause the flu." While the statement on the

web site was ultimately changed, it was not changed until AFTER the media ran with the erroneous information. These statements created damaging misperceptions of FluMist and its benefits AND almost certainly reduced the number of people protected against this year's flu epidemic that included the virulent mismatched Fujian strain. "Accurate" educational materials from our public health officials are paramount to successfully sharing the benefits of vaccination to the general public and achieving broad immunization against the flu.

How is MedImmune contributing to efforts to prepare for a pandemic threat?

- First and foremost, we have already made a considerable investment – to the tune of $1 billion - to overcome the extraordinarily high regulatory hurdles facing new vaccines in order to make available an important new option for influenza vaccination.
- Second, should we ultimately choose to remain in the flu vaccine manufacturing business, we will undertake the financial burden of spending hundreds of millions of *additional* dollars to hopefully expand our indication to include persons younger than 5 and older than 49 years – which if we successful in doing, will in turn hopefully increase the demand for FluMist that will then justify increasing our manufacturing output to capacity.
- Third, we are working proactively with federal authorities to develop and test a FluMist vaccine for use in a pandemic situation.
- And fourth, we have worked closely with the World Health Organization to make MedImmune's intellectual property in the area of reverse genetic engineering available for development and testing of inactivated pandemic vaccines.

So in conclusion, the core of my message to you today is that in 2004, in the wealthiest and most powerful country on earth with the world's best healthcare system, it should be unacceptable to all of us that more than 100 American children and countless elderly have recently died from a completely preventable disease. Importantly, this year is not unique. EVERY year 36,000 Americans die as a result of the flu. The best way for us to be prepared to prevent this from happening in the future – as well as to help make sure we are prepared to deal with a pandemic situation – is to have the current flu vaccination recommendations expanded to include all Americans, and especially expanded to include that all healthy children be vaccinated against the flu.

Thank you for this opportunity to speak with you today.

Chairman TOM DAVIS. Thank you very much.

Dr. Hearne.

Dr. HEARNE. Good morning. I am Shelley Hearne with the Trust for America's Health, which is an independent organization working to prevent epidemics and protect people. And thank you, Chairman Davis and Mr. Waxman, for holding this important hearing. It is certainly a timely one. Just last week we were reminded, with the ricin scare on Capitol Hill, as to how vulnerable we are for many health threats. Fortunately, no one was killed in this incident, at least this time, but it could have been worse.

One of the things that happened in the anthrax event of 2001 was the rampant scare around the country, which overwhelmed our public health system. That could have happened here with ricin, and if it had we would have been in worse shape. In part, public health is not prepared for a variety of health threats. Just take a look at the public health laboratories. Most labs cannot test for ricin, and the majority of them do not have a chemical weapon response plan.

So I know we are at an influenza hearing, and you may ask me what has this got to do with the flu. It is actually everything. One of the things we certainly know is that mother nature can rival the best of terrorists out there. We have had 35,000 people routinely die from the flu, and if a pandemic came along, we certainly learned this in 1918, it can kill hundreds and thousands of more people.

So is it possible to prepare for the threat of bioterrorism and at the same time to effectively prevent, contain, and reduce an influenza pandemic? Unfortunately, it is not the kind of public health system that we currently have today, but I would argue is just the defense system that we need. However, America is very far away from reaching that goal.

In December, our organization released a report, "Ready or Not? Protecting the Public's Health in the Age of Bioterrorism." We found that 2 years after the September 11th attacks, and almost $2 billion in new Federal funds, we have made a lot of progress in preparing for public health, and that has been echoed certainly with the panels today, but there is much more that needs to be done.

For example, we found that CDC and the majority of States do not have pandemic flu plans. This, coupled with minimal oversight of Federal and State strategies, shows a failure to translate our concern about bioterrorism into a comprehensive strategy for public health preparedness. Another major finding is that only two States were prepared to distribute and administer emergency vaccination or antidotes from the strategic national stockpile. And while significant improvements have been made in the labs, only six States report that they have sufficient facilities should a major public health emergency occur.

Finally, our report revealed that since the September 11 attacks, two-thirds of the States have cut their State public health budgets. And now the President's 2005 proposed budget threatens to compound the impact of those cuts by slashing support for State programs. As has been noted before, this includes cutting the State and local bioterrorism preparedness by $105 million. Overall, CDC

is facing a 3 percent budget reduction, just at a time when we need this agency to be even stronger.

To stop the hemorrhaging of the Nation's public health infrastructure, we are recommending a series of "fixes" to move us toward that modern system with the capacity to fight a multitude of hazards. Rather than concentrating solely on bioterrorism or responding to each "disease du jour" crisis, public health preparedness efforts must be focused on all hazards. We need to simultaneously address the potential for biological, chemical, radiologic, and natural disease outbreaks. TFAH is recommending that the CDC authorize States to use Federal preparedness funds to support an all-hazards approach. CDC must work with the State and local health officials to define measurable and mandatory preparedness standards. State or local governments must demonstrate to CDC that core public health funding levels are met, thereby ensuring the maintenance of effort. We believe that Congress should make a long-term investment toward biosecurity and authorize an independent review to determine whether current expenditures are sufficient.

Let me add that the Trust for America's Health conceptually does support the President's Bio-Surveillance system and also upgrading the Bio-Watch Program, but we do not believe it should come at the expense of funding for State preparedness initiatives, which have been cut by 11 percent. We also endorse increasing the discretionary programs in the public health service by 12 percent. At a time when U.S. health care spending averages about $1.7 trillion, we believe that public health programs that prevent, control, and treat disease are essential to reducing America's health care bill.

Last, we recommend that Congress, in consultation with the President, convene a summit to develop a cohesive national approach to public health protection. We need a blueprint for the 21st century, and the summit should address all threats to our Nation's health, including chronic diseases, infectious and animal-born illnesses, food safety, and terrorism. Whether it is anthrax or the avian flu, public health defenses must be fortified, not forfeited. To do otherwise would guarantee only chaos and a staggering loss of life should a public health emergency occur.

Thank you for the time and for being part of this public policy debate.

[The prepared statement of Dr. Hearne follows:]

Written Testimony of

SHELLEY HEARNE, DrPH
Executive Director
TRUST FOR AMERICA'S HEALTH

Before the

UNITED STATES HOUSE OF REPRESENTATIVES
COMMITTEE ON GOVERNMENT REFORM

February 12, 2004

MOVING TOWARD "ALL-HAZARDS" PUBLIC HEALTH PREPAREDNESS

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Good Morning. I am Dr. Shelley Hearne, Executive Director of Trust for America's Health (TFAH), a non-profit, non-partisan organization dedicated to saving lives by protecting the health of every community and working to make disease prevention a national priority. I would like to thank Chairman Davis and Ranking Member Waxman and the entire Government Reform Committee for holding this important and timely hearing. On behalf of Trust for America's Health, I appreciate the opportunity to testify on these matters of health and homeland security and will be happy to respond to any questions members of the Committee may have.

The attacks of September 11 and the anthrax killings that followed alerted Americans to the danger our nation faces from terrorists armed with biological, chemical or radiological weapons. Sadly, with the recent discovery of ricin on Capitol Hill, we have been reminded of our vulnerabilities again.

In recent years, we have also seen the resurgence of a far different threat, but one which is no less lethal: infectious diseases, which, if left unchallenged, could easily become pandemics endangering the lives of millions of American families.

Preventing -- and combating -- these and other health hazards is the unique responsibility of our public health system. As Americans we have long taken special pride that our nation has set the pace for disease prevention and control worldwide. But today America's public health system is being stretched to the breaking point.

In fact, even as it is given new responsibilities in the War on Terrorism, America's public health system is still struggling to carry out its peace time mission.

Without question, Americans agree that protecting public health is one of the principal responsibilities of government. However, after more than two decades of neglect, it is increasingly apparent that the public health system is woefully unprepared to meet the challenges it faces today, let alone new public health dangers in the future.

Recent opinion research sponsored by our organization and the American Cancer Society revealed that a majority of Americans believe that investing in public health is vital to improving homeland security. They are, of course, correct.

However, that same poll also found that Americans were more worried about the current flu epidemic than they were of the risk of bioterrorism. Americans are correct in that regard, too.

Because while a bioterrorist event could have catastrophic consequences, many public health specialists are far more concerned about what some describe as the "inevitable" outbreak in this country of a lethal strain of influenza. They know that, despite our best efforts to produce vaccines to cover the most likely strains of the flu virus, nature always has the potential to serve up particularly virulent variations that have the potential to spread swiftly and severely leaving a broad swath of sickness and death in their wake.

Anyone who has seen the suffering caused by an earthquake, tornado or hurricane understands that the destructive power of Mother Nature rivals that of even the best armed terrorist. Disease outbreaks can be far more devastating. Annually, the flu kills 35,000 people in this country. Yet, as we learned in 1918, a flu pandemic could kill hundreds of thousands more.

Prior to 9/11 and the anthrax attacks, officials concerned about the threat of bioterrorism used to talk about pandemic flu planning as a good model for bioterrorism preparedness. Now, the opposite is the case; bioterrorism preparedness receives most of the attention and certainly the vast majority of new funding. The bad news is that today the U.S. public health defenses are not adequately prepared for either threat.

Last year, TFAH released a report, *Ready or Not? Protecting the Public's Health in the Age of Bioterrorism*. We found that two years after the September 11 attacks and almost $2 billion in new federal funds later, progress has been achieved in state preparedness for public health emergencies. However, much more needs to be done.

For example, the TFAH report, issued in December 2003, found that CDC and the majority of states lack a pandemic flu plan. Though 13 states have provided their plans to CDC, remarkably there is no formal process to ensure an adequate and coordinated response by public health agencies. This lack of preparation for a flu epidemic, coupled with the lack of oversight of federal and state strategies, indicate a general failure to translate the concern over bioterrorism into a comprehensive strategy for public health preparedness. Last year, other critical infrastructure gaps also became apparent as the country struggled with an average flu outbreak: vaccine shortages, uncertain distribution chains and an inability to track childhood influenza deaths.

Yet, despite this and other shortcomings, the TFAH report revealed that, since the September 11 attacks, two-thirds of the states cut their public health budgets. Now, the President's proposed budget for FY 2005 threatens to compound the impact of those reductions by cutting integral programs to our health defenses, including the state and local bioterrorism preparedness support to states. This $105 million dollar decrease in federal support to the states, when combined with the substantial reduction in state support, places our public health defenses at serious risk.

To stop the hemorrhaging of the nation's public health infrastructure, TFAH is recommending a series of "fixes" to move us toward a modernized public health system that is prepared to combat a multitude of hazards. Whether it's anthrax or avian flu, America's public health defenses must be fortified, not forfeited. To do otherwise would guarantee only chaos and a staggering loss of life when a major public health emergency eventually occurs.

The Nation's State of Preparedness

Over the course of the last year, TFAH conducted a state-by-state assessment of public health improvements and remaining vulnerabilities. We examined 10 key indicators in three general categories: funding; public health infrastructure; and "double duty" indicators that reflected the status of states' traditional public health programs, like responding to annual flu epidemics or ensuring food safety.

We found that the funds provided by Congress over the past two years have been crucial to help jump start some very important improvements. Our report found that progress has been made in most states to improve communications with the public and between health agencies. Every state had at least an initial plan on paper of how to mobilize public health resources in the event of a terrorist attack. Additionally, several states have been able to make preliminary upgrades to laboratory equipment and facilities, and hire the necessary staff to operate the advanced equipment.

Yet, the report found that there is much room for improvement. For example, only six states report that they have sufficient laboratory facilities should a major public health emergency occur. These findings build on those of an earlier TFAH report, *Public Health Laboratories: Unprepared and Overwhelmed.* Our review of state public health laboratories found that there is a pervasive lack of clear direction on planning and protocols needed to deal with a chemical weapon attack. According to Scott Becker, the Executive Director of The Association of Public Health Laboratories (APHL), "Only eight state public health laboratories have a chemical terrorism emergency response plan in place. We do not have testing methods or a lead agency for many of the laboratory activities that will be needed when a crisis occurs." This observation is even more alarming in light of the recent ricin incident.

Additionally, TFAH identified other serious vulnerabilities and areas requiring significant improvement. While the federal funds were going to the states, we found that nearly 66 percent of states, facing budget crises, had cut their public health funds over the same time period. TFAH also found that there is a serious workforce crisis including a shortage of trained public health specialists and epidemiologists. According to the Health Resources and Services Administration (HRSA), currently fewer than 50 percent of the nation's 500,000 public health professionals have had formal, academic training in public health. Further, CDC data shows that 78 percent of all local health department executives do not have graduate degrees in public health.

Another major concern was our finding that only Florida and Illinois are fully prepared to distribute and administer emergency vaccinations or antidotes from the national stockpile. This situation is complicated by the fact that many states had planned to rely on the National Guard to help with stockpile distribution, but many National Guard units have now been called to duty overseas. The report also showed that states' readiness for other health emergencies, such as major infectious disease outbreaks like severe acute respiratory syndrome (SARS) is seriously inadequate.

I should point out that the TFAH's December 2003 study employed a set of 10 key indicators to measure progress, which were selected with an advisory committee of state and local health officials and public health experts. These indicators offer a snapshot of the public health readiness. TFAH is not suggesting that the indicators present a complete picture of preparedness. Instead we believe they represent a framework policymakers can use to hold federally funded public health programs accountable. TFAH believes that, in the final analysis, the CDC, in consultation with state and local health officials and outside specialists must define measurable standards for preparedness for hazards ranging from anthrax, to ricin, to influenza.

What Can the U.S. Do Now to Better Prepare for the Flu, Bioterror, and a Full Array of Health Hazards

The American public health community has a solid understanding of many actions that should be taken to make our country more safe and secure. However, achieving a battle-ready public health defense at the federal, state and local levels will take years of sustained commitment, funding and oversight.

TFAH believes that rather than concentrating solely on bioterrorism or responding to each "disease du jour" crisis individually, public health preparedness efforts must be focused on an "all-hazards" approach. We can and should maximize and leverage our investments in public health at the federal, state, and local levels.

To achieve the optimum all-hazards approach to public health preparedness, TFAH's specific recommendations include:

- CDC must formally authorize states to use federal preparedness funds to support an "all-hazards" approach to preparedness that simultaneously addresses the potential for biological, chemical, radiological and natural disease outbreaks.

- CDC, in consultation with state and local health officials and outside experts, must define measurable standards for comprehensive preparedness that all states and major local health departments should meet.

- Congress should provide long-term commitment and oversight toward ensuring the nation achieves adequate and sustainable public health security. As such, Congress should authorize an independent review to assess whether current expenditures -- at the federal, state and local levels -- are sufficient.

- Health security requirements must be established, including mandates and accountability measures to ensure all citizens are adequately protected.

- CDC must be required to track state and local funding and expenditures on critical public health functions, particularly those involving federal support. Unfortunately, there is mounting evidence to indicate that severe state budget cuts dilute the impact of the federal preparedness investment. Concerned that federal

dollars should supplement -- and not supplant -- state and local funding streams, Congress urged the Health and Human Services Secretary to guard against such actions, but this "maintenance of effort" needs to be enforced.

- CDC should independently verify that health emergency performance standards are being met at the federal, state and local levels.

PUBLIC HEALTH: RETURN ON INVESTMENT

Nothing is more sacred than protecting the health and safety of all Americans. In this regard, Congress should continue its commitment to bolstering our public health defenses. Given the wide range of health threats facing the United States, now is not the time to cut funding for public health, nor is it time to divert funds allocated to CDC's state and local preparedness capacity-building grants to new initiatives.

Specifically, while TFAH supports the President's Bio-Sense Initiative and expanding and upgrading the BioWatch program, we do not believe it should come at the expense of funding for state public health preparedness initiatives. An effective public health system is vital to our national security and, if they are looked at as an integral part of the public health defense, Bio-Sense and BioWatch have the potential to help thwart attacks and save lives. Accordingly, TFAH maintains that the $130 million allocated to CDC's Bio-Sense Initiative should be added to, not taken from, the capacity building line items in the CDC budget.

Moreover, as the nation's leader for disease control and prevention, every health department looks to the CDC for guidance on health concerns ranging from Alzheimer's to West Nile virus. Underfunding this vital agency seriously compromises our nation's health defenses and homeland security. TFAH is deeply concerned about the proposed cuts, totaling nearly three percent of the agency's total budget.

Over the course of the last year alone, local, state, and federal health officials have responded -- and contained -- the SARS, monkeypox, flu, and West Nile virus outbreaks, and the recent ricin incident in the Senate, while simultaneously struggling to address the everyday health needs of all Americans. It is imperative to enhance, not reduce CDC's budget.

For this reason TFAH endorses the efforts of the Campaign to Increase Function 550: a coalition of over 370 organizations, urging Congress to increase the discretionary programs of Function 550 (the Public Health Service) by 12%. At a time when U.S. health care spending averages $1.7 trillion annually, TFAH believes that funding public health programs that prevent, control and treat disease is essential to reducing America's health care bill. For this reason, TFAH believes that bioterrorism preparedness efforts should complement, and not compete with the other national health priorities such as battling cancer and heart disease.

What's more, the American public agrees. Our January 2004 poll revealed that more than three in four Americans say the government needs to spend more on health priorities and as stated earlier, a majority of respondents felt that public health spending was vital to improving homeland security.

CONCLUSION

The current effort to improve America's ability to respond to a public health emergency represents a major organizational challenge. Whatever the threat, an effective response depends on the functioning of a patchwork of state and local public health agencies, whose funding sources, structure and responsibilities can vary significantly from state to state and even county to county.

It is clear that the U.S. needs a more cohesive public health system. Though we are not suggesting that state and local agencies be subsumed by a new national body, we do believe public health officials at all levels should initiate a process that leads toward common goals and a clear understanding of the role of each entity in reaching them.

The President, in consultation with Congress, should convene a White House summit that will develop a concrete vision for the future of the American public health system and the resources needed to make it a reality. This summit would consider how our country can build a robust, integrated public health infrastructure. TFAH believes that such a summit could craft a blueprint for a public health system that is designed to meet both America's current and emerging health threats. The discussion must include how to develop a public health system for the 21st century – the summit should address all aspects essential to public health, such as bioterrorism, chemical, and radiological preparedness, known and emerging infectious diseases and chronic disease prevention and control. At the same time, we believe it could foster a long-overdue dialogue about the resources required to implement needed changes and guarantee accountability at every level of the public health system.

Once again, thank you for allowing TFAH the opportunity to contribute to the policy debate on public health preparedness. I am happy to answer any questions.

Chairman TOM DAVIS. Thank you all. Thank you all very much.

Let me start, Dr. Young, with you. Four million doses were destroyed last year. Was that the effect of the fact that the target population, those under 5 and over 50, that your doses were not recommended for them, or do you think it was the misinformation that was put out on some Web sites, or a combination? I mean, clearly those doses could have been used by people between 5 and 50, instead of some of the other doses that were used from other areas, and the reallocation we would have had, in theory, I would think, 4 million more doses available to people and might have saved some lives.

Dr. YOUNG. Absolutely. I think there were a number of factors that contributed to that. But it wasn't without our trying to get the vaccine out. We actually had discussions with the CDC in December about giving them a million doses, take them free; we are going to throw them out anyway. Take it free, you can have it. They said, we can't use that many doses; maybe we could take 250,000 doses. They never came back and took those doses from us. But we tried our best.

Chairman TOM DAVIS. I bet you, Dr. Stroube, and Mrs. Miller can use them in your areas, right? I mean, I think you hit the problem in terms of the distribution of this. Maybe we didn't see the problem at that point, either, developing the way it developed.

Dr. YOUNG. It was actually the day before Christmas, well into the epidemic.

Chairman TOM DAVIS. Keep going, I didn't mean to interrupt.

Dr. YOUNG. No, I think there are other issues about misperceptions, misconceptions, the public health authorities not getting behind this new innovative vaccine. You even heard today talk about how the inactivated vaccine, it was your question, is only about 70 to 90 percent effective when the strains are matched, only about 30 to 50 percent effective when the strains are mismatched. We have data in our package insert from a clinical trial we did in children that the first year of the vaccine, when tested in those kids, was 95 percent effective. That was when the strain was matched. And the second year, when it was not matched, 87 percent efficacy.

Chairman TOM DAVIS. Do you think the nasal is more effective?

Dr. YOUNG. It is an afterthought of the public officials to talk about that vaccine. It is a great vaccine, yet it is sort of in the category of hand washing.

Chairman TOM DAVIS. Just to give you your day here, do you think the nasal is better than the ordinary vaccine, more effective for the target populations that you are looking at?

Dr. YOUNG. We haven't done head-to-head trials. In fact, those trials are underway right now. We actually expect to unblind a couple of trials in a couple of weeks, and we plan on doing another head-to-head trial. All I can tell you is we have the data in children that shows that it is between 80 and 96 percent effective. I don't know that such data exists to show that kind of efficacy with the inactivated vaccines.

Chairman TOM DAVIS. The only thing I can say is we have three producers of flu vaccines, and if you go out, it makes it a lot tougher.

Dr. YOUNG. Well, it is hard to justify staying in the business and hemorrhaging money left and right.

Chairman TOM DAVIS. Oh, I understand. Let us continue to work.

Dr. Pien, let me ask you. Of course, you are in the business as well. The one thing that concerns us is not anything that you are responsible for, but that is if there is a pandemic around the globe, the fact that your manufacturing sites are in Britain. Is there any way that you have to serve Great Britain or Europe first, and not America, that would limit your ability to disburse those?

Go ahead and answer that, and then I have another followup.

Mr. PIEN. Mr. Chairman, I would say that this is really a subject of some speculation. We have no knowledge that the government of Great Britain would actually restrict the flow of the products. And all we can do, of course, knowing that this is something outside of our control, if it should arise, is to do our best to increase the total production capacity and make the investment to enable it, and that is both in terms of the conventional egg-based technology as well as flu cell culture flu, as I mentioned before in my testimony.

Chairman TOM DAVIS. I think it is to our advantage to keep everybody in business.

How much does it cost to put a dose together in each case, once the basic research is done, then to develop the dose and decide how much you are going to do? You get some economies of scale there, but this year we fell behind because it takes a period of time, I guess, to work a batch up. Is that the correct understanding?

Dr. YOUNG. Yes, that is correct. By the time you actually get the strains, optimize the growth of the strains in the eggs, and then produce, test, have the FDA review and release the product, it is many months, upwards of 6 months or more.

Chairman TOM DAVIS. But once you have gotten one batch done, isn't it cheaper and faster to do the second? You don't have to go back and do basic research.

Dr. YOUNG. No, you don't have to go back and do basic research, but the timeline for production, testing, and release is the same for every batch. Now, in terms of the cost, I can tell you that the cost per vaccine is driven in large part by the level of manufacturing you are doing. For us to just turn on the lights in our plant costs $60 million, if we don't even make a single dose of vaccine. And until we actually get up to the point where we are above 4 or 5 million doses at the current retail price, we don't make a single dime on the product until we are above that; and you don't get down into really reasonable margins until you are up in the range of 15 to 20 million doses of production. So there is a certain fixed amount of cost that we have no matter how many doses we produce.

Chairman TOM DAVIS. But the economies of scale mean the more you produce, the cheaper, basically.

Dr. YOUNG. The more you produce, the cheaper it is.

Chairman TOM DAVIS. Is that the same?

Mr. PIEN. I would generally concur with Dr. Young's comment, except to amplify a few points. First of all, you have to make ongoing capital investments to keep up with the ever-rising standards

of quality control which the FDA insists on, and has the right to insist on. One of the reasons that we are making this $100 million investment is precisely for the reason of wanting to bring state-of-the-art capacity to the buildings and the machinery and so on, such that as the standards rise for quality control and quality assurance, we make the products that meet those standards.

I would also say that there is a general perception that the vaccines are probably less profitable than pharmaceutical products. I think the real reason for this is because every year you have to make new products, and every vaccinee, as it were, is a new patient; there is no refill as you would have for any hypertensive, for example. So these are issues that do contribute to profitability.

I think most of us who are in the vaccine business, and are remaining in the vaccine business, understand that it is part of our social covenant that if we have the technology, we have the know-how, vaccinology is one of the most important ways that medicine can make a contribution to human health care and to the country's overall protection.

Chairman TOM DAVIS. What is the shelf life of an average dose? Dr. Young, you talk about destroying maybe 4 million doses. Is that because they are not usable in the next year?

Dr. YOUNG. Yes. Actually, the shelf life is mandated by the FDA that it expires on June 30th, after the season, so that there is no misuse of the wrong vaccine the following season after the strains have changed.

Chairman TOM DAVIS. OK, that is the FDA's ruling.

Dr. YOUNG. That is correct.

Chairman TOM DAVIS. But as a practical matter, if you were to put this in a refrigerator and store it, would it still have potency 5 years later if that strain came back?

Dr. YOUNG. You would need to store it, in our case, because of a live vaccine, you would need to store it frozen at very cold temperatures, and it has a very long shelf life. But the problem is, as you heard from Dr. Fauci, the strains must be updated every year for the ones which are in circulation, so this year's vaccine probably isn't going to be very effective next year.

Chairman TOM DAVIS. No, it wouldn't be, but 5 years from now it could come back, couldn't it?

Dr. YOUNG. Usually that doesn't happen. It is very rare that the same strain will actually reemerge back into the population, because everyone is immune to it. They have already seen it, so the virus is tricky enough to figure out that the only way it can continue to circulate in the population is it has to change to the point where no one's prior immunity can protect them against that strain.

Chairman TOM DAVIS. Even if you have a regional outbreak here, that is just the way it works.

Dr. YOUNG. That is just the way it works.

Chairman TOM DAVIS. OK. I understand that.

Dr. Hearne, in your testimony you said States are experiencing a shortage of trained public health specialists and epidemiologists. How serious is this crisis?

Dr. HEARNE. Well, it is actually getting worse because we are finding that the pipeline doesn't exist for many of the epidemiolo-

gists or technical staffers, particularly in Virginia which has built one of the top labs in the country, but is seeing problems with work force and the ability to pay highly skilled, highly trained people. That is just one area of the gaps that we are seeing. Certainly there have been improvements in communications in some of the other areas, but there are still also gaps in making those labs even better, doing some of the better disease surveillance; number of holes that continue to need to be filled.

Chairman TOM DAVIS. OK.

Dr. Stroube, do you have any thoughts on that?

Dr. STROUBE. Well, we have been fairly lucky. The lab is a little bit harder to do because you are looking usually for Ph.D.s that are really state-of-the-art, and there is a demand for those. In finding epidemiologists, we actually created 140 new positions in the health department using the Federal money on it, and we put an epidemiologist in every health district in the State, we have 35 of them, and planners. And we had some difficulty recruiting, but we have been fairly successful in doing that. Part of it, we are close to a lot of public health schools and we have a fairly attractive place to recruit people in, so we have done pretty well in trying to recruit people. But that is a long-term consideration we have been thinking about, and we have been working with public health schools and trying to get more people trained in the way we need them.

Chairman TOM DAVIS. You also mentioned in your testimony that not all of the Virginia health care workers were immunized this year with the flu vaccine. I guess we ran out of it through the process?

Dr. STROUBE. We ran out in December, just suddenly. We were going great guns. Like I said, we put a lot of emphasis on flu this year, and part of it was to be prepared for SARS. It is hard to distinguish flu from SARS, so the more people we have immune to flu, the easier the job dealing with SARS, we thought it would be. So we really put a lot of effort into that and we started immunizing everybody in the health department, nursing homes, hospitals, and really pushed hard on that.

Chairman TOM DAVIS. Well, let me ask you and I will ask Ms. Miller and also Dr. Hearne. We really are not ready for prime time if you get a pandemic at this point, is what I gather from the first panel and this. Obviously we are making strides, we are getting better each year we get a test, but is that fair to say?

Dr. STROUBE. Well, I think the biggest problem is vaccine availability on it. For 3 out of the last 4 years we have not had adequate flu vaccine supplies; it has either been late due to manufacturers dropping out, and we just haven't had the material that we need to be able to enact a pandemic flu plan to get people to do that. Until we have the flu vaccine, plans aren't really effective.

Chairman TOM DAVIS. Did you use any of the nasal vaccine?

Dr. STROUBE. We used some of the nasal.

Chairman TOM DAVIS. For part of the population?

Dr. STROUBE. For part of the population. It started becoming available to us at the discounted price later in the game on it. Part of the problem we have with that, we have health departments all across the State, and as Dr. Young said, you have to maintain that

at a very low temperature, which is a little hard for us to do in distribution systems.

Chairman TOM DAVIS. But we have to get better at it, obviously, the way you are going.

Ms. Miller, do you have any comment on that?

Ms. MILLER. I would just comment that local governments have a limited amount of dollars to buy vaccine with, and so I don't know what the cost is between the two differences, but I would like to ask Dr. Allan if she could just comment on that, if that had an effect on why the FluMist was not used effectively.

Chairman TOM DAVIS. Sure. We have sworn her in. Let us hear from her.

That will be my last question, then I will yield to Mr. Waxman.

Dr. ALLAN. At the local level, the implementation of an expanded influenza vaccine program this year was a real challenge. The vaccine supply issue has been a concern for several years, as Dr. Stroube mentioned. Beyond that, though, we ended up putting twice as much staff time into doing the flu vaccine program this year as we normally do, and I can't frankly tell you whether that was a success or not from a public health perspective, because those staff were doing influenza vaccines which needed to be done, instead of doing care to pregnant women or routine other vaccines to children or investigating hepatitis, which also needed to be done, because we do not have any cushion, any expansion in our staffing. So to hit a surge like something like influenza means that we are stopping other things that are also affecting the health of the communities in maybe less dramatic, but probably just as important a way.

So I think our program, for example, declined the FluMist vaccine because we had already made an extra outreach to the high-risk populations, which we do consider our primary responsibility, and we had no more staff time just to give the lower-risk people the vaccine. We tried to let the private doctors know it was available. We couldn't have done any more than we did, having already doubled the staff commitment to this program at a cost to others.

Chairman TOM DAVIS. OK. Thank you very much.

Mr. Waxman.

Mr. WAXMAN. Dr. Stroube, in your written testimony you stated Virginia does not include the pneumococcal vaccine in its childhood immunization program. Is this vaccine important and is it recommended, and what are the implications of Virginia not including this vaccine in its immunization program?

Dr. STROUBE. The Prevnar vaccine, which is pneumococcal for children, has been recommended by the Federal authorities for several years now, but it is an expensive vaccine and we have been unable to afford to give it to all the children that need it, and so that makes them at risk of pneumococcal diseases such as pneumonia and ear infections.

Mr. WAXMAN. What are the lessons of this experience for the new recommendation to provide flu vaccine to young infants?

Dr. STROUBE. I think any time there is a recommendation to expand or bring in a new vaccine, it has to come with money, because there just isn't any money available. We are looking at the vaccine purchase appropriations increasing by 50 percent since 1999, but

yet the cost of giving a child all the recommended vaccines has increased by over 125 percent. So we are falling behind, particularly every time we get a new vaccine.

Mr. WAXMAN. Well, it is troubling to realize that the President is proposing to make permanent tax cuts for the richest Americans, but his budget can't fund the childhood immunizations adequately.

Are you going to find yourself making progress under this proposed budget or are you going to fall backward?

Dr. STROUBE. Well, we will do the best we can under what we have and prioritize what we do and try to use all the funding we can both from the State and Federal Government to meet the needs as we see them.

Mr. WAXMAN. I wonder if I can direct some questions to Dr. Susan Allan, if you would.

Dr. ALLAN. Absolutely.

Mr. WAXMAN. The General Accounting Office is reporting today that the smallpox vaccine program has diverted resources from core public health activities. Do you agree this diversion has been a concern at the local level? And if so, can you give us any examples?

Dr. ALLAN. The smallpox vaccine program took a tremendous amount of concentrated effort. I am actually speaking at a conference next week on this, and the title of my presentation is, "Making Lemonade From A Box of Lemons." Dr. Stroube already mentioned I am in the State of Virginia here, and we have two staff with all of the Federal money, with the commitments required at the State level for the labs and technologies and other things. At the local level we had enhancement by two staff in our health department. It took 22 people the equivalent of a week's time just over the first couple months of the smallpox program, plus 3 of us essentially full-time for 4 months just for the startup implementation of this. So the cost in terms of redirecting our resources was considerable.

Now, we tried. We are good public health people. We tried to turn this into general principles of infection: education, disease control, certainly enhancement with our relationship with the doctors and hospitals. So there were some benefits to this, but the cost to our system was a major disruption for a full 6 months.

Mr. WAXMAN. That is interesting, because Secretary Thompson assured us there would be adequate Federal funding for the smallpox program, and what we are hearing is that this program may have actually undermined some core public health activities.

Dr. ALLAN. If I may add a point, the Federal money came to the States with, in effect, a contract. It is a grant process, so the States had pre-committed, as we did in our role with the States, to what would be done with the money that came. So we already had a full workload agenda that used all of the resources provided, and then the smallpox program was dropped on top of that. Compensation was provided after the fact, but we don't run the local budget by going in the hole. So we didn't create extra expenses for that, we cut other commitments. So by the time, at least for many of us, that the Federal money came, it was too late to do any good, whereas if it had come with the commitment, there might have been some value.

Mr. WAXMAN. Well, obviously this was, I would think, an unintended consequence, and I am interested in your view. The administration's budget is investing heavily in bio-surveillance technologies. Are there any potential unintended consequences to Federal efforts to detect bioterrorist agents in the environment? And in the event of false positive results, could these efforts generate more work and divert State and local officials from core public health activities?

Dr. ALLAN. A number of our communities have already had experience. A lot of the military establishments and some post offices have had this. Here in the National Capital region, the Anacostia Post Office had a false positive on an anthrax test just a couple months ago, in November. Arlington had three post offices that were shut down until we knew for sure that was not a true positive, that it was in fact a bad test result.

Meanwhile, there were 10 of us who spent the equivalent of almost a day and-a-half full time on this, and we put together a treatment clinic for the postal workers because we didn't know whether they had been exposed or not. We had 90 staff we brought in on overtime and set up a clinic to treat them, for one false positive. Rough estimate of the cost to us was about $10,000 for that one false positive test. And these technologies are untested and unproven; they generate a lot of errors that, every time there is a hit on these systems, we are going to have to drop whatever we are doing and investigate them. So, you know, it is like having a smoke detector. If you don't have a fire department to respond and see if it is a real fire or not, what is the point of the smoke detector?

Mr. WAXMAN. Dr. Hearne, I understand Trust for America's Health is a nonpartisan and nonprofit organization that focuses on the need for a robust public health system in this country. From your perspective, what, if anything, concerns you about the President's fiscal year 2005 budget?

Dr. HEARNE. Part of our concern has been just at a time when we have had a series of wake-up calls—the flu outbreak was just the beginning, we have had, since then, the avian flu, certainly SARS before, anthrax and ricin last week. We are getting bombarded with a number of very strong wake-up calls that our public health system is a critical part of our homeland security. But in fact what we have found in our investigation is that it probably is the weakest link in homeland security. What concerns us is there are a number of gaps that we have identified and now is the last time that you should be considering cuts to this budget, when in fact there are very specific initiatives that need to be advanced, particularly to protect us from all flanks. And so just the fact the word "cut" is being used in the same sentence as CDC is troubling.

Mr. WAXMAN. I understand you have a score card of State preparedness, and the scorecard revealed that even as the Federal Government was increasing resources for public health, many States have cut their public health funding. How important is it to track actual spending on public health by States and localities? And as far as you know, is the CDC tracking actual spending by States and localities? And is it troubling that even at the same time the administration is proposing to cut public health funding

for States, it is failing to closely track actual spending on necessary activities?

Dr. HEARNE. Let me try to break that down in a few ways. One, our report did find that approximately two-thirds of the States were opening up the back door, they were removing funds from their critical public health programs just at the time when Federal funds were coming in, which risked diluting the important investments that the Federal Government was making. That is disturbing. The even more troubling point in this, as you were raising concerns about accountability, we were not able to get this information on State expenditures and investments on the public health side from CDC. In fact, we have received a number of calls from CDC to have our data because they would like to know. It is important that they are asking to know, but they should have known this for a long time because certainly as one is looking to purchase better protection and safety for the American citizens, you need to know where your money is going; you need to know what you have bought. And the fact that there has not been that accountability measure, one, you can't track what is happening in the States, you can't compare one State's activities to another.

We actually had to contract with the National Conference of State Legislators to get this data, which we are happy to provide to CDC, but it should be a routine matter of tracking and accountability. Just as we should be tracking diseases in this country, we should also track where the money is going.

Mr. WAXMAN. Thank you.

Mr. Pien, from your perspective, what can the Federal Government do to support the quickest possible development of pandemic flu vaccine?

Mr. PIEN. Mr. Waxman, as I testified before, I think that one of the most important aspects of the private-public partnership has been that of the advancement of technology and sciences. In this regard, if we are going to be able to advance the funding level with the National Institutes of Health, or at least keep it at a level that can perpetuate these kinds of partnerships, it would go a long way.

Second, I think that the considerations of how we appropriate resources such that we can enhance the level of natural growth in demand will go also a long way to the ability for manufacturers in toto to be able to steadily increase their investment and increase their capacity.

So the collaboration between the private sector in thinking about how they can propagate the messages about the seriousness of the disease that flu represents, along with the funding that the CDC and all of the States and municipal and county agencies that preside over infrastructure that will get the vaccines into the arms of the people who need it, I think that will go a long way to prepare the country's readiness for pandemic.

Mr. WAXMAN. I want to thank all the panelists for their presentation.

Mr. Chairman, I wonder if we could keep the record open for a short time to see if we can elicit further responses in writing from some of the witnesses.

Chairman TOM DAVIS. Well, some offered to do that. We will keep the record open for that. And in addition to that, we had some

witnesses who couldn't come who submitted written testimony, and that will be put in the record.

I want to thank our witnesses today. It has been very helpful to us. I want to thank you for your testimony.

I want to thank the committee staff that worked on this hearing, and we are adjourned.

[Whereupon, at 12:31 p.m., the committee was adjourned, to reconvene at the call of the Chair.]

[The prepared statement of Hon. Congressman Elijah E. Cummings and additional information submitted for the record follow:]

Statement of Congressman Elijah E. Cummings
House Government Reform
Full Committee Hearing
"A Review of This Year's Flu Season: Does Our Public Health System Need a Shot in the Arm?"
February 12, 2004 at 10:00 a.m.
2154 Rayburn House Office Building

Thank you, Mr. Chairman.

I want to thank you for holding this hearing to examine this year's flu season in an effort to assess our nation's preparedness to deal with a pandemic.

As you are well aware, Mr. Chairman, Congress has appropriated several billion dollars since September 11th in our effort to enhance public health preparedness. Despite our efforts during, this flu season the United States was ill-prepared for the early and severe outbreak of influenza that managed to claim the lives of 129 youth, as reported by the CDC on February 5, 2004. All of these victims were under the age of 18, and 54 of them had already received the flu vaccine.

The high demand for the flu vaccine among children and elderly, our highest risk population, coupled with media coverage and heavy publicity of this year's flu epidemic, led our nation to a vaccine shortage. To this shortage, I

ask, what must be done to ensure that our nation is prepared not only for unexpected strains of the flu virus, but also for adequate production of the flu vaccine?

On a broader scope, in the event that our nation is hit with a deadly outbreak of contagious disease, like the SARS outbreak that affected China, we must also be prepared to safeguard our citizens by providing them with either the proper treatment for a disease or a prophylaxis to prevent infection. Because of this, it is pertinent that we analyze whether new techniques and incentives are needed to guarantee that effective and safe vaccines, drugs, and diagnostic tools are developed speedily.

I also note that the President's FY 2005 Budget includes a 3% cut in the CDC budget and at the same time diverts over $100 million from state public health preparedness activities to a bio-surveillance program. I hope that in your testimonies, you will address how such a funding cut would affect our nation's ability to prepare for possible contagious outbreaks. Congress understands that if we are to expect excellence of our public health preparedness, then we must provide the proper means by which this can be accomplished.

With that said, I look forward to hearing from our witnesses and once more thank you, Mr. Chairman, for holding this hearing.

Written Statement of Congressman Nathan Deal
"A Review of This Year's Flu Season:
Does Our Public Health System need a shot in the Arm?"
Committee on Government Reform
February 12, 2004

I commend Chairman Davis for continuing his series of hearings to examine the state of our public health preparedness, using this year's flu season as a case study. The same public health infrastructure that is engaged during a routine flu season would also be relied upon in a naturally occurring pandemic or a bioterrorist attack. If our constituents are to feel confident in our abilities to handle a bioterrorist attack, we should certainly be able to rise to the challenges of each flu season.

In particular, I would urge the Committee and our witnesses to consider ways to leverage the logistics and distribution expertise within the private sector to track, deliver, and assist with redistribution of vaccine where needed. Through discussions my staff has had with representatives of Henry Schein Inc., the largest supplier of flu vaccine to office-based practitioners, it is clear that the distributor community plays an important role in our public health preparedness. It is my understanding that Schein will be submitting a written statement, which I would ask be included in the Committee's hearing record. Distributors track quantity and location of vaccines shipped to their customers. Distributors routinely manage vaccine supplies for states and ship flu vaccine on a same day basis, as directed by the CDC, to targeted state and local health departments. Distributors provide vaccines and supplies directly to health care providers, an important non-governmental component of the public health system.

As we prepare for potential shortages in future flu seasons, pandemic flu, or even a bioterrorist event, a partnership between vaccine manufacturers, distributors, the government, and doctors is needed to address issues in the supply chain, from the manufacturing process to the health care providers who administer the shots. This partnership should utilize the logistics and distribution expertise in the private sector, to ensure that we have the capability to distribute vaccine in the most efficient delivery network possible.

WRITTEN TESTIMONY

PROVIDED BY

AVENTIS PASTEUR

BEFORE THE HOUSE GOVERNMENT REFORM COMMITTEE

REGARDING INFLUENZA VACCINE PLANNING AND PREPAREDNESS

FEBRUARY 12, 2004

INTRODUCTION:

Aventis Pasteur is pleased to offer this testimony to the Government Reform Committee of the United States House of Representatives. We are the largest and most experienced manufacturer of influenza vaccine in the United States. We also have extensive experience in both national and global emergency public health preparedness. Our experts have partnered with the government and the private sector community for more than 30 years to meet both routine and emerging pandemic needs for the United States' national influenza immunization preparedness. This includes responding during times of national emergency, such as our supplying tetanus vaccine to New York following the events of September 11, 2001 and our donation of smallpox vaccine in the wake of the bio-terror attacks of October 2001. Aventis Pasteur has definitive ideas on how to better align America's demand for and supply of vaccines, and we welcome the chance to provide this testimony.

As we approach pandemic planning and assess the effectiveness of annual influenza vaccine processes, Aventis Pasteur believes certain steps are necessary to maximize preparedness. First, public officials should ensure that efforts to increase demand for influenza vaccine – and thus drive increased supply – are consistent and predictable. Second, given that the current vaccine production process relies on chicken eggs, flock protection planning is an essential component of preparedness planning. Last, with the predictable onset of a pandemic, public health officials should take necessary steps to ensure an adequate supply of vaccine based upon existing technologies and current economic factors, while reasonably looking to the long-term development of alternative technologies, such as cell-based vaccines.

A. Background

Aventis Pasteur is the largest company in the world devoted entirely to vaccines. We are the world leader in the development and manufacture of influenza vaccines. We have a history of proven, effective, licensed, manufacturing processes for influenza vaccines and are also working to introduce innovative cell culture and administration devices into vaccine manufacturing.

Aventis Pasteur produces in the United States about half of the nation's annual influenza vaccine supply. Each year, our facility in Swiftwater, Pennsylvania, produces approximately 50 million doses of flu vaccine, representing over half of the doses of flu vaccine sold in the United States. As a global vaccine manufacturer and leading supplier of vaccines and biologicals in the United States and throughout the world, Aventis Pasteur's primary focus is vaccine development and commercialization. Each year more than 500 million people are immunized with an Aventis Pasteur product. Worldwide, Aventis Pasteur produces 98 unique biological products that combat 20 different diseases: These include:

- Bacterial Diseases – tuberculosis, diphtheria, *Haemophilus influenzae* b, meningococcal meningitis, whooping cough, pneumococcal infections, tetanus, typhoid fever and cholera
- Viral Diseases – measles, mumps, poliomyelitis, rubella, yellow fever, influenza, hepatitis A, hepatitis B, rabies, Japanese encephalitis and chickenpox.

Aventis Pasteur has extensive experience in bringing vaccines to license in the U.S. regulatory environment. Aventis Pasteur currently has 20 U.S. licensed vaccines and has received eight FDA approvals since 1987, seven of which occurred in the 1990s.

Aventis Pasteur has three research and development units and four manufacturing sites, including a major influenza production site in Swiftwater, Pennsylvania. We also have access to a Level 3, Bio-Safety laboratory as well as research and development and manufacturing

facilities in France. These dispersed centers of excellence provide great flexibility in the assignment of facilities and resources to specific development and manufacturing programs.

As mentioned above, during the terrorist attacks on September 11th, Aventis Pasteur came to the immediate assistance of the government and the American public. Within 24 hours of the attacks on the World Trade Center and the Pentagon, Aventis Pasteur donated 50,000 doses of Tetanus vaccine to relief efforts in New York and New Jersey. Following the Anthrax attacks of October 2001, Aventis Pasteur donated approximately 85 million doses of smallpox vaccine to the U.S. government's emergency preparedness stockpiles. Last year, we donated our proprietary Vero cell line to help the US government quickly study the SARS virus. We were subsequently awarded a NIH contract to develop a SARS vaccine. Our company annually works with FDA to produce the annual influenza vaccine and also have governmental partnerships to develop vaccine against potential pandemic strains.

Aventis Pasteur has proven itself as a leader in immunization and as a responsible corporate citizen in the United States and around the world. We will continue to work closely with the federal government, as a full partner in addressing this country's inter-pandemic and pandemic flu needs.

B. Annual Planning and Vaccine Production

Each year, more than 36,000 Americans die from influenza and related complications. While influenza immunization has long been considered a public health priority and is included in DHHS' Healthy People 2010 goals, the nation has a long way to go to achieving target immunization levels. As DHHS Secretary Tommy Thompson recently acknowledged, by far the best way to achieve increased annual supply of influenza vaccine - and to ensure adequate capacity in the event of a pandemic – is to increase the number of Americans receiving annual

influenza immunization from the current levels of 70-80 million people to, at least to the Healthy People 2010 goal, of 150 million people vaccinated on an annual basis. Such planning also includes working with the Centers for Medicare and Medicaid Services (CMS) to ensure our elderly and our citizens who receive health care through public assistance are adequately protected.

Of special note is the vulnerability of important risk groups including health care and other essential workers, as well as young children. We encourage increased emphasis on implementing approaches to raise demand to better prepare Americans for emergency response in general. Last week, we presented several such suggestions in testimony to the National Vaccine Advisory Committee (NVAC) at the Department of Health and Human Services. The specific recommendations for increasing influenza immunization demand are attached for the committee's consideration.

Egg-based influenza vaccine has been produced at the Swiftwater site for decades through a proven, rigorous, FDA-licensed process. This includes production of vaccine during the 1976 pandemic influenza campaign, as well annual inter-pandemic production. Efficient and timely manufacture of a quality influenza vaccine requires effective management of fertilized chicken eggs, virus growth, harvest and purification processes, the filling of finished vaccine into vials, and an efficient distribution system. The Swiftwater site has world-class capability in each of these areas.

The process starts with diligent efforts to maintain the quality of chicken flocks producing fertilized eggs at farms distributed across Pennsylvania. Aventis Pasteur manages the selection of farms, administers precise quality control and quality assurance procedures, and provides constant monitoring in conjunction with contracted chicken farmers. Back-up supplies

of fertilized eggs are also maintained to react quickly to any disturbance in our primary supply. The flock and egg management techniques contribute to the quality and robustness of the subsequent manufacturing steps.

Aventis Pasteur maintains a Seed Development Laboratory within the Swiftwater campus where skilled scientists have developed effective techniques to pass and freeze the selected virus strains to produce influenza virus that will grow rapidly within the fertilized eggs. These techniques have been refined since the early 1970's and contribute to the high yields seen in Aventis Pasteur's manufacturing process.

As you are aware, there is national concern about a potential shortage of influenza vaccine in this country as a result of early outbreaks that received extensive media coverage during this year's flu season. Aventis Pasteur is one of only of two companies that supply the US market injectible influenza vaccine, and the only company licensed in the United States to manufacture injectible vaccine. As such, we are uniquely positioned to provide you with the facts from an industry perspective on this topic to address any lingering concerns.

Each year Aventis Pasteur decides, after consultation with the Centers For Disease Control (CDC), the Food and Drug Administration (FDA) and the World Health Organization, how much influenza vaccine to produce. That number is based on a range of factors, to include the year's pre-bookings for sale of the product, plus a generous additional quantity in anticipation of later orders that we produce out our own financial risk. Influenza vaccine is reformulated every year for the upcoming flu season. The product is licensed annually and influenza vaccine that cannot be sold has to be destroyed. In 2002, Aventis Pasteur made 48 million doses of the vaccine, and sold only 43 million doses. The remaining five million doses had to be destroyed. In 2003, the company made and distributed 43 million doses of influenza vaccine- at some risk

to the company – since only 32 million doses were ordered during the traditional pre-booking season. The forecasted demand for 2003 was dramatically down from the previous year.

To better understand how we produce influenza vaccine, it is important to explain the process involving egg production. Specially bred flocks of chickens produce the fertile eggs used in the growth of the influenza virus and tens of millions of these eggs are used each year to produce the vaccine. The virus strains have to be separately grown in these eggs. As a result of the time necessary to undertake this process, production takes several months. While a number of companies- including ours- are working on new technologies for producing influenza vaccine, these technologies are a number of years away from being practical for vaccine production due to the scale needed to satisfy growing demand.

Typically influenza vaccine is trivalent; that is, it contains three different strains of the influenza virus. These strains are selected each year by the Federal government in consultation with global public health agencies. Strain selection is based on global surveillance. While history has demonstrated that, in most years, the "predictions" of what strains will circulate in the world are accurate, strains may change or mutate as occurred this year.

This year the question has been asked as to why more vaccine was not produced. The answer is actually quite simple. The amount of vaccine produced is based on the assumption of demand and the best predictor of demand is last year's level of demand. Our experience tells us that the severity of the previous season is a main driver of consumer demand. Any vaccine produced above demand has to be destroyed. As an annual licensed product, it cannot be stockpiled. This is why the real solution is to increase long-term influenza demand in the United States, so that vaccine is not wasted.

To put the planning for this past flu season in perspective, in 2002, insufficient demand resulted in manufacturers discarding 12 million doses intended for U.S. market. Also, for the 2003 season, as late as November 2003, all indications were that vaccine orders in 2003 were down significantly, indicating demand would be less than in the prior season. As discussed earlier, influenza vaccine production is based on pre-book vaccine orders plus an "at risk" allowance. Again, if Aventis Pasteur is unable to sell the influenza product, it will be destroyed.

Beginning in early December 2003, early influenza outbreaks - and the widely reported deaths of children from influenza in Colorado and Texas - created unanticipated vaccine demand after the production was finalized. Ample supply from all manufacturers had existed up to the third quarter of 2003 (roughly, 83-87 million doses). Unanticipated and unprecedented demand in late November/early December exhausted supplies.

Aventis Pasteur proactively notified CDC of this late surge as soon as it was detected. We worked with CDC to reserve/allocate the remaining additional vaccine doses to states where the outbreaks were most serious. Aventis Pasteur offered the CDC 100,000 additional doses of Fluzone® Influenza Virus Vaccine and 150,000 doses of Fluzone®, Pediatric Influenza Vaccine that it had in reserve.

With respect to planning for the 2004-2005 flu season, pre-booking orders will once again drive vaccine production, thus proving again that demand drives supply. The 2004-05 season will be the first following the recent ACIP recommendation to vaccinate children between the ages of six and twenty-three months of age. Aventis Pasteur began accepting pre-booked vaccine orders for 2004-2005 season on December 1, 2003.

If orders for influenza vaccine are "pre-booked" and ordered early, all stakeholders will benefit. In accordance with the goals set forth in Healthy People 2010, the objective is to

significantly increase immunization across all high-risk groups. Congress should fully support these 2010 goals and the initiatives needed to meet them. While there is no need for legislation to address this issue (since it is not a matter of legal authority, but simply one of implementation), Congress should properly use its oversight responsibilities to ensure these goals are achieved by 2010 or before to help address any concerns about availability of flu vaccine in an inter-pandemic year.

C. Pandemic Planning

It is generally accepted that the best way to plan for a Pandemic event is to increase annual inter-Pandemic influenza immunization rates. Nearly every informed public health professional fully anticipates that an influenza pandemic event will occur at some point in time. As defined by the World Health Organization, an influenza pandemic occurs when a new influenza virus appears against which the human population has no immunity, resulting in several, simultaneous epidemics worldwide with enormous numbers of deaths and widespread illness. With the increase in global transport and communications, as well as urbanization and overcrowded conditions, epidemics due to a new influenza virus are likely to quickly take hold around the world. During the past century, four influenza pandemics have been documented: the Spanish Flu (A/H1N1) of 1918, the Asian Flu (A/H2N2) of 1957, the Hong Kong Flu (A/H3N2) of 1968 and the Russian Flu (A/H1N1) of 1977. The most significant of these, in terms of mortality, was the Spanish Flu of 1918 with an estimated 30-40 million deaths worldwide. Seroarcheology further suggests that influenza A/H2N2 and A/H3N8 pandemics also occurred in 1889 and 1900. The emergence of avian strains in Hong Kong (A/H5N1) in 1997; again in 1999-2003 (A/H9N2), and today's news regarding (H5N1), remind us again of the constant threat of pandemic influenza. The obvious conclusion is that an influenza pandemic event is

inevitable and requires carefully coordinated planning between the government and private sector.

As discussed above, current large-scale industrial technology for production of influenza vaccine requires growing the influenza virus strains within fertilized chicken eggs, harvesting the fluids from the eggs, deactivating and splitting the virus within the collected fluids, and purifying the fluids to isolate the appropriate components that will provide immunogenicity. A continuous secure supply of appropriate quality, fertilized eggs is necessary to secure the supply of flu vaccine.

The Fiscal Year 2004 Omnibus Appropriations Bill, which includes DHHS' funding, appropriates $50 million "to ensure a year-round influenza vaccine production capacity and the development and implementation of rapidly expandable influenza vaccine production technologies." In press interviews, DHHS Secretary Tommy Thompson has stated that this money should be used first to increase the supply of the chicken eggs necessary to manufacture flu vaccine in the event of a surge in demand for a pandemic. *See e.g., Wall Street Journal* (December 17, 2003). Aventis Pasteur fully supports these objectives.

Safeguarding a timely supply of appropriate quality eggs is a basic requirement to managing a pandemic. Significantly, it takes in excess of ten months to establish a new supply of eggs should the existing supply prove unacceptable for whatever reason. Aventis Pasteur's approach would ensure that sufficient fertilized eggs of the appropriate quality could be produced at any time throughout the year. We foresee no technical difficulty in developing and protecting this supply chain.

Aventis Pasteur is prepared to partner with the federal government to accelerate its manufacturing abilities and research and development projects to satisfy the surge requirements

of the nation during influenza pandemic. Aventis Pasteur, annually, works closely with several public agencies to provide influenza reagents, sera and antigens. In collaboration with the government, Aventis Pasteur tests novel influenza strains on its proprietary cell lines to be used in testing and manufacturing. Although the influenza vaccine market is primarily private, Aventis Pasteur has supplied the government with more vaccine than any other influenza vaccine manufacturer to date.

An important point to remember is that 85% of the influenza vaccine distribution in the United States is distributed in the private sector. Approximately 15% of doses are sold in the public sector. The current private system is robust and effective, and it is important to build on the existing private-public sector distribution system in a Pandemic event, rather than seeking to change or modify the system.

Aventis Pasteur has also called on the Federal government and DHHS leadership to engage the provider community to induce greater immunization demand and to assure that Medicare, Medicaid and private health insurance encourage influenza immunization. Again, most experts agree that an influenza pandemic event with grave public health consequences is long overdue and that current planning is inadequate to meet demands for a pandemic influenza vaccine.

Most recently, Aventis Pasteur is prepared to meet the additional influenza vaccine demand expected as a result of the recent CDC Advisory Committee on Immunization Practices (ACIP) recommendation to immunize infants, ages 6-23 months. In addition, Aventis Pasteur has assumed a prominent role at the annual Influenza Summit established by the AMA and CDC. The Summit's message is consistent with the Healthy People 2010 goal, to increase inter-pandemic influenza vaccination annually in order to immunize 150 million US citizens by 2010.

Since only between 70-80 million Americans are currently immunized against influenza in the United States, these efforts are aimed at building inter-pandemic demand and infrastructure thus ensuring pandemic preparedness.

D. Conclusion

Engineering plans for our new influenza vaccine facility will double our influenza vaccine production capacity in Swiftwater, Pennsylvania. This will be the largest facility of its kind in North America. Aventis Pasteur has long recognized that influenza vaccine is a critical U.S. health need and has been this country's corporate leader meeting this important health need. Influenza vaccine has been manufactured at the Swiftwater site since 1972, including since 1997 by Aventis Pasteur. Our continuing investment has made Aventis Pasteur the highest volume, and most consistent manufacturer for the US market today. Aventis Pasteur has consistently proven itself the leader in producing flu vaccine at the highest efficiencies in industry and it has demonstrated the proven commitment to do what is necessary to meet the health needs of the US public and federal government.

Aventis Pasteur

APPROACHES TO INCREASE NATIONAL DEMAND FOR ROUTINE INFLUENZA IMMUNIZATION

Increasing Influenza Vaccine Demand to Meet Healthy People 2010 Goal

In 2003, the late season spike in influenza vaccine demand demonstrated the need to develop a national consensus in the United States about how to predictably increase the annual demand for influenza vaccine immunization. Influenza vaccine immunization is important because it protects America's public health. Increased demand will drive increases in the annual vaccine supply. The focus on influenza immunization demand is essential to achieve Healthy People 2010 goals and to effectively plan for a Pandemic event. Aventis Pasteur, as charter member of the Influenza Summit's public-private partnership, and the global leader in influenza vaccine development and production, suggests the following steps to increase influenza immunization. Aventis Pasteur welcomes additional suggestions. Among specific points Aventis Pasteur recommends:

1) **Best Practices:** Encourage practitioners, managed care organizations, insurers, health care institutions, and community-based immunizers to develop, share, and implement best practices to run seasonal surge adult/pediatric immunization campaigns. This begins with timely pre-ordering and may include flexible scheduling of patients, periodic reminders from physicians, and implementation of standing orders to offer immunization to meet patient care quality objectives.

2) **Annual National Awareness and Educational Campaigns:** Support public health authorities, the National Influenza Summit, advocacy organizations and coalitions to manage sustained, annual public awareness/education programs. These programs should convey consistent information about high-risk groups, articulate key influenza recommendations to the public, and communicate information regarding the timing and length of the influenza immunization season. Programs should also be tailored to "at risk" target groups, including minorities.

3) **Support HHS Agencies to meet their annual influenza immunization goals as a unified Department including:**

   a. **NVPO**: Gain consensus of public and private partners about national immunization goals, and convene annual reviews of progress to objectives for supply and demand goals.

b. **CDC:** Support annual widespread practitioner and public education and awareness campaigns and advocacy coalitions; add routine publication of adult/pediatric influenza immunization rates by risk group and states to help target and measure specific improvements.

c. **CMS:** Annually inform all Medicare and Medicaid providers and other parties about influenza recommendations, coverage and reimbursement and the importance of early pre-ordering to implement successful seasonal campaigns. Publish adequate and timely reimbursement notices for providers and make available Medicare immunization rate information to public health to measure further improvement.

d. **FDA:** Support FDA to continue to provide timely, current technical expertise and oversight to ensure vaccine safety, the timely availability of vaccine, and to further boost public confidence in vaccines.

4) **Extend Immunization Season:** Consider expanding the immunization season into December and possibly beyond.

5) **Emphasize Exemplary Healthcare Worker Immunization Efforts:** Identify and resolve barriers to health care worker immunization by emphasizing the responsibilities to protect oneself, one's patients and one's family. Provide workers with information designed to educate patients year-round concerning influenza and immunization.

6) **Insurers/Managed Care Providers:** Secure agreement among managed care/insurance companies about the importance of covering influenza immunization and administration; ensure that managed care system, health care professionals, relevant institutions, and all immunizers understand the need to Pre-Order vaccine; and remind at-risk patients why immunization is so important and implement standing orders.

7) **Strategic Influenza Vaccine Reserves:** Immediately establish shared risk reserves for influenza vaccine to ensure protection for unforeseen outbreaks and/or in the event of a Pandemic. Influenza vaccine cannot be stockpiled from year to year, but government negotiations with the private sector of an annual strategic vaccine shared risk reserve could offer the public, and health care providers, additional confidence that supply will meet ever increasing demand.

Proposed by Aventis Pasteur, February 2004 to the National Vaccine Advisory Committee, Washington D.C.

February 19, 2004

Delivered via Facsimile: (202) 690-8425

Julie Louise Gerberding, M.D., M.P.H.
Director
Centers for Disease Control and Prevention
1600 Clifton Road, N.E.
Mail Stop D-14
Atlanta, Georgia 30333

Dear Dr. Gerberding:

On behalf of the Committee on Government Reform, we want to thank you for testifying at our recent hearing, "A Review of This Year's Flu Season: Does Our Public Health System Need a Shot in the Arm?" Although the hearing was thorough, we have additional questions that require your response.

After listening to the second panel's testimony, we would like you to answer the following questions:

1. Dr. Shelley Hearne of Trust for America's Health testified that the Centers for Disease Control and Prevention (CDC) does not track actual spending at state and local levels on public health preparedness. Is this true? How does CDC assess the resources available at state and local levels?

2. Medimmune testified that existing influenza vaccine recommendations are too narrowly targeted and Chiron testified that increasing the number of Americans vaccinated in non-pandemic flu seasons would help expand vaccine capacity for a pandemic. The current influenza vaccine recommendations cover people under the age of two and over 50 and include people who have underlying medical conditions that put them at high risk. Are the current influenza vaccine recommendations adequate or do they need to be expanded?

3. Dr. Robert Stroube, the Virginia State Health Commissioner, testified that the President's budget does not fully fund the recent recommendation for influenza immunization of babies six to 23 months. How much would it cost for all states to be able to provide this vaccine through their public vaccination programs?

4. Dr. Susan Allan of the Arlington County Health Department testified that bio-watch and/or bio-surveillance programs could drain significant local public health resources in the event of false positives. What is CDC's estimate of the additional costs to state and local governments of deploying systems that could have false positives?

Thank you again for your participation in our recent hearing. We request a reply to this letter by March 11, 2004. Please deliver your response to Brien Beattie, Deputy Clerk, Committee on Government Reform, U.S. House of Representatives, 2157 Rayburn House Office Building, Washington, D.C., 20515.

Sincerely,

Tom Davis
Chairman

Henry A. Waxman
Ranking Member

CDC Follow-up Questions

1. **Dr. Shelley Hearne of Trust for America's Health testified that the Centers for Disease Control and Prevention does not track actual spending at the state and local levels on public health preparedness. Is this true? How does CDC assess the resources available at state and local levels?**

   The Trust for America's Health testimony looked at the CDC and HRSA bioterrorism preparedness cooperative agreement. For this particular agreement, CDC has numerous tracking mechanisms for budgeting and spending at state and local levels. Every CDC grantee has two points of contact for technical assistance - a grants management official from the Procurements and Grants Office (PGO), and a Project Officer from the Division of State and Local Readiness (DSLR). PGO is the official accounting arm of the CDC, and applies the Department of Health and Human Services Grants Management rules to each cooperative agreement released from CDC. According to grants management rules, each CDC awardee is required to submit end-of-year financial statements (Financial Status Reports - FSRs) that indicate the amounts each grantee obligated in each focus area. CDC follows standard grants management rules and requires grantees to provide written justifications for most re-directions, carry-over and supplemental requests to the budget. The requests are recorded and tracked in electronic systems that both the Procurement and Grants Office (PGO) and the Division of State and Local Readiness (DSLR) access as part of regular grants management.

   CDC also tracks programmatic progress through two required progress reports - one due six months into the budget period, and one at the end of the budget period.

   In addition, CDC and HRSA terrorism preparedness funds were given a special account at the HHS payment management system which allows a dollar for dollar accountability of expenditures. The figures provided through the Payment Management System (PMS) allow CDC to monitor the total amount of funds "drawn down" to pay for program expenses, although not defined in class/object categories or by focus area. Through this monitoring, CDC determines what the special fiduciary needs of each state are and helps make recommendations to the states about managing and properly accounting for all their funds.

2. **Medimmune testified that existing influenza vaccine recommendations are too narrowly targeted and Chiron testified that increasing the number of Americans vaccinated in non-pandemic flu season would help expand vaccine capacity for a pandemic. The current influenza vaccine recommendation cover people under the age of two and over 50 and include people who have underlying medical condition that put them at high risk. Are the current influenza vaccine recommendations adequate or do they need to be expanded?**

The current influenza vaccine recommendations target persons at greatest risk of influenza-related complications. Persons not targeted can receive influenza vaccine if they wish to reduce their chances of influenza infection.

Based on the influenza seasons of the past two years, when pediatric deaths have been reported and modeling data which suggest that an average of approximately 92 children aged <5 years die from influenza-related complications, it is appropriate to reassess the current recommendations, particularly as they relate to children. Analyses that should be done include an estimation of the burden of severe disease in children of all ages, the risks and potential health benefits of vaccination, the acceptability of yearly vaccination of children, and the cost of expanding such programs.

The Advisory Committee on Immunization Practices (ACIP) discussed this issue on February 24, 2004 and is considering whether revisions may be appropriate. There is concern that public demand would outpace production capability.

3. **Dr. Robert Stroube, the Virginia State Health Commissioner, testified that the President's budget does not fully fund the recent recommendation for influenza immunization of babies six to 23 months. How much would it cost for all states to be able to provide this vaccine through their public vaccination programs?**

Influenza vaccine was recommended for routine use in children aged 6 – 23 months in October 2003. Approximately $23 million is being provided in FY 2004 Vaccines for Children (VFC) program funds for the new recommendation. However, no additional Section 317 program vaccine purchase funds were appropriated in FY 2004 and the President's budget request represents level funding in FY 2005. CDC estimates that the new recommendation will cost the states in the range of $7 - $14 million, depending on how quickly they are able to implement the recommendation.

In the recently passed budget, $40 million dollars in VFC stockpile funds were allocated for the pediatric influenza vaccine stockpile. Unlike most stockpiled pediatric vaccines, the influenza vaccine formulation is changed each year so the stockpile will have to be replenished on a yearly basis. Because the 317 program was level funded, there will not be additional discretionary funds available to immunization grantees to purchase the stockpiled influenza vaccine in the event of a major outbreak again. That will limit the use of readily available federal pediatric vaccine funds to children eligible for the Vaccines for Children Program and private sector children through manufacturer repurchase. If states had more 317 vaccine purchase funding, they too could benefit from the stockpile. However, since immunization projects have insufficient funding to fully support routine childhood immunization recommendations for 317-eligible children and most states are having budget difficulties at this time, some children

seeking immunizations in public sector settings will not benefit from the influenza stockpile.

Since states are not receiving additional discretionary 317 vaccine purchase funds, many may have to implement two-tier influenza policies, meaning they could not provide flu vaccine to non-VFC eligible children and/or underinsured children who go to public health clinics for vaccination.

4. **Dr. Susan Allan of the Arlington County Health Department testified that bio-watch and/or bio-surveillance programs could drain significant local public health resources in the event of false positives. What is CDC's estimate of the additional costs to state and local governments of deploying systems that could have false positives?**

The BioWatch program to date has not had a true false-positive event. There have been preliminary screening tests that upon confirmatory testing have been determined to be false preliminary signals. State and local health departments are provided with resources (staff, equipment and supplies) for the BioWatch program so as not to impact the day to day functioning of the laboratory. If there were significant numbers of true false positives, then the greatest impact would be on the epidemiologic and surveillance branches of the health departments since they would have to investigate these reactions. It is not possible to estimate additional costs since the BioWatch program has not had any of these problems.

Enhanced surveillance programs do require additional effort from local resources; however, since these are usually done in response to an "event", they are short-lived and should not require significant financial and personnel resources.

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