H1N1 PREPAREDNESS: AN OVERVIEW OF VACCINE PRODUCTION AND DISTRIBUTION

JOINT HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH

AND THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

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CONTENTS

WITNESSES

H1N1 PREPAREDNESS: AN OVERVIEW OF VACCINE PRODUCTION AND DISTRIBUTION

WEDNESDAY, NOVEMBER 18, 2009

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH, JOINT WITH THE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittees met, pursuant to call, at 10:07 a.m., in Room 2123, Rayburn House Office Building, Hon. Frank Pallone, Jr., [chairman of the Subcommittee on Health] presiding.

Present: Representatives Waxman, Dingell, Pallone, Eshoo, Stupak, Engel, Green, DeGette, Doyle, Harman, Schakowsky, Gonzalez, Baldwin, Ross, Weiner, Matheson, Barrow, Christensen, Castor, Sarbanes, Murphy of Connecticut, Space, Sutton, Braley, Whitfield, Shimkus, Blunt, Buyer, Pitts, Walden, Sullivan, Murphy of Pennsylvania, Burgess, Blackburn, and Gingrey.

Staff Present: Kristin Amerling, Chief Counsel; Bruce Wolpe, Senior Advisor; Karen Nelson, Deputy Committee Staff Director for Health; Ruth Katz, Chief Public Health Counsel; Sarah Despres, Counsel; Stephen Cha, Professional Staff Member; Allison Corr, Special Assistant; Mike Gordon, Chief Investigative Counsel; Dave Leviss, Chief Oversight Counsel; Erika Smith, Professional Staff Member; Ali Neubauer, Special Assistant; Karen Lightfoot, Communications Director, Senior Policy Advisor; David Kohn, Press Secretary; Jen Berenholz, Deputy Clerk; Matt Eisenberg, Staff Assistant; Alan Slobodin, Minority Chief Counsel, Oversight; Ryan Long, Minority Chief Counsel, Health; Aarti Shah, Minority Counsel, Health; Karen Christian, Minority Counsel, Oversight; and Kevin Kohl, Research Analyst.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. The meeting will come to order.

Today we are having a joint hearing of the Health Subcommittee and the Oversight and Investigations Subcommittee, and the hearing is titled H1N1 Preparedness, an Update of Vaccine Production and Distribution.

We are going to begin with opening statements from the members of the subcommittees. The chairman and ranking members of the two subcommittees will be recognized first for a 5 minute opening statement, followed by 5 minute statements by the Chairman and ranking member of the full committee and the Chairman

Emeritus. Other members of the subcommittees will then be recognized for 2 minute opening statements. I am going to begin by recognizing myself.

Let me explain that the purpose of this hearing is to get an update from the main stakeholders involved in the manufacturing and distribution of the H1N1 vaccine and to shed some light on where we currently are in the process and what we can expect moving forward.

The most recent estimates from the Centers For Disease Control are truly alarming. Over the past 6 months, it is likely that 22 million people in our country have been infected with the disease and about 98,000 have been hospitalized. To date, it is estimated that 3,900 individuals have lost their lives to H1N1.

Unlike regular flu that affects predominately the elderly population, the vast majority of H1N1 deaths have occurred in people between the ages of 18 to 64. Even more tragically, the CDC estimates that 540 of these deaths have occurred in children. These numbers are significantly higher than earlier estimates, and as we move further into flu season, we can only expect to see them increase even more.

We now know that this virus and vaccine is unlike flu vaccines that we have produced before in it is extremely difficult to grow. Early estimates on vaccine amounts were based on how vaccines usually behaved in the production phases. Unbeknownst to anyone involved in this process, H1N1 proved to be very different, and though the manufacturers have been able to speed the growth of the vaccine by selecting the fastest growing strains, we still are lagging behind where we originally thought we would be with our production numbers.

Fortunately though, this particular vaccine appears to be highly effective in creating an immune response in individuals, and for adults, one small dose of the vaccine will produce enough of a response to protect from H1N1. But these early delays in production are now rearing their ugly head as our country watches the disease spread and take lives while vaccine is still hard to come by.

To date, nearly 42 million doses are available for distribution, which is about half of what we originally expected to have by this time. It is no wonder therefore that story after story in the papers and on the news highlights the frustration that the American people are facing in trying to get the vaccine that will protect them from the disease. We hear accounts of individuals waiting in line for hours at clinics, some cannot find clinics in their neighborhood at all, and areas are still waiting to receive even the first doses of the vaccine.

There is a school district in my hometown, for example, that is yet to receive the vaccine, and understandably the parents are irritated. And this frustration is exacerbated by accounts of places in the country that seem to have more than enough vaccine in some areas, where getting this vital protection from H1N1 poses no difficulty at all. So we are getting a lot of disparities from one place to the next, and, naturally, people are confused and they are angry.

So that is why myself and Chairman Stupak are holding this hearing today. I personally would like to better understand how the production of vaccine is going; when, for example, we will be

able to expect enough vaccine so that all individuals who want it can get it; and will this happen before flu season is over.

I would also like to understand more about the distribution process. I understand that the States make their own distribution plans and do the ordering for their States through the CDC. But how are these plans created and how do States make the determination where to start with vaccine distribution and which distributors to prioritize?

We have a number of very important individuals with us today who have been working around the clock on these issues, and I would like to welcome you all. We appreciate your taking the time to provide us with this update today.

We understand how difficult this process has been. We are not here to beat you up, but we are here to try to get some answers, and particularly where we go from here.

With that, I would like to let me just thank again Bart Stupak, Chairman Stupak, for working with me to put this hearing together.

I guess we are going to go to Mr. Walden at this point for an opening statement.

OPENING STATEMENT OF HON. GREG WALDEN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF OREGON

Mr. WALDEN. Thank you very much, Mr. Chairman, and thank you for convening this important hearing.

H1N1 has been dominating the news and parents and the general public's concern for the last couple of months, as we all know. I am hopeful this joint subcommittee hearing can help answer questions and discuss solutions to the challenges arising from the first flu pandemic in 40 years.

As many of you, I have firsthand experience with H1N1. I think I was probably the first Member of Congress to go on record as being diagnosed as likely having H1N1. I had not been vaccinated, because, like the majority of my fellow Members of Congress, I don't fall into the CDC's priority groups. And like millions of other people across the country who have had H1N1, I felt rotten for a few days. It is not something you want and it is not something you want to pass on to others. But I did follow my doctor's advice and the CDC's directions and stayed home here in D.C. to rest for at least 2 days after my fever broke, which is what I was told do to do. Luckily, I was fortunate and recovered quickly.

Others have not been so fortunate. Last week, we learned that approximately 4,000 people, 540 of them children, have died from H1N1. The fact that this flu hit young children so hard and the constant news reports about rising pediatric deaths have scared the daylights out of parents.

You see this fear played out in the number of parents lining up with their small children at public vaccination clinics for hours at a time and flooding their pediatricians' offices with phone calls trying to hunt down the vaccine.

From the folks I hear from in my district, they can't find the vaccines. Based on statements made by HHS and CDC, parents had counted on being able to vaccinate their children by October or November. Originally CDC projected 40 million doses would be avail-

able by the end of October. Ultimately, only 23 million doses were available. Instead, parents hear reports every day on the news about rising pediatric deaths and vaccine shortages and delays. Some wait in line for hours, only to be told when they get there, there is no vaccine left.

Today, I hope we can get some concrete answers about when the vaccine will be available. I also want to hear from HHS and the vaccine manufacturers about the reasons for the delay and what can be done now in and in the future.

HHS Secretary Sebelius was before the full Energy and Commerce committee on September 15th, and at that time she testified by mid-October a "large-scale campaign" for vaccinations would be underway. She also stated repeatedly that there would be "enough vaccine for everyone." Secretary Sebelius now says the vaccine manufacturers painted an overly rosy picture of their production. Is that the case, or did the virus seed not perform as expected?

I don't think finger pointing exercises are particularly helpful at a time when we are facing one of the biggest public health issues in recent years and a somewhat panicked public. But there have been repercussions, no doubt about it.

I also want to learn about how HHS has assisted States and local health departments in preparing for this pandemic. For example, in my district, hospitals are implementing their incident command plans due to emergency rooms being hit with waves of patients with flu-like systems. These spikes of patients are coming at a time when doctors, nurses and hospital staff are either home sick with the flu or taking care of their children that are home from school because of the flu.

So we are looking at a situation of increased patient volume and decreased staff capacity. Hospital administrators are monitoring staff levels and patient volumes in some cases on an hourly basis so if they reach a tipping point, the hospitals can cancel elective surgeries to ensure there is adequate staffing to care for patients in the emergency room and those admitted to the hospital.

When I called the 18 hospitals in my district, each one of them asked, where is the vaccine that we were told was coming? So let's get the facts on the table about the reasons for the delay and when HHS knew about it; if there were production issues, how can they be corrected; and if there are communication issues between the manufacturers and HHS and HHS and the public, how they can be fixed so parents are not unnecessarily confused?

When the administration promised enough vaccine for everyone, the people want to know that it is coming. I am very interested to hear from Dr. Lurie and Dr. Schuchat about what direction HHS and CDC have given hospitals in how to prevent this confusion in the future.

So I hope this isn't the last hearing we have on this issue. This is the first pandemic in 40 years and the first since Congress began providing funding starting in 2006 for pandemic preparedness. At that time, we were deeply concerned about the possibility of a pandemic spreading a bird flu that could be 40 percent in mortality. Fortunately, this one has not proven to be as deadly. I believe Congress has appropriated $13 billion for this effort. This is an area

where we need continued oversight so we can figure out what worked, what didn't, and what we should do going forward.

So I am particularly interested in the technologies for vaccine production and whether we can do better in the future. I understand that one of the manufacturers, MedImmune, has been able to meet its delivery schedule, in part due to the different kind of technology that company uses to make a live attenuated vaccine. Even though MedImmune grows the virus in chicken eggs, which is uncertain and unpredictable in yielding a sufficient supply, they have received better results.

I know that as part of its pandemic preparedness planning, HHS has awarded contracts to companies to look into cell-based vaccine production, as well as other ways to improve yields and production times. So I would like to know about the status of these efforts and whether we are doing enough to ensure that we are prepared for a pandemic influenza.

I welcome the witnesses and look forward to discussing these important public health issues with them. Thank you for your testimony.

Thank you for the hearing, Mr. Chairman.

Mr. PALLONE. Thank you, Mr. Walden.

Chairman Stupak.

OPENING STATEMENT OF HON. BART STUPAK, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. STUPAK. Thank you, Mr. Chairman, and thanks for working with me and our O&I staff in putting together this hearing. I look forward to doing this joint hearing today. I think we have a good hearing lined up. As you said, we are not here to point fingers but try to find out how we can do things better in the future.

Today, we continue our committee's oversight of the 2009 pandemic H1N1 flu by examining more closely the production and distribution of H1N1 vaccine. This will be the third hearing the Energy and Commerce committee held this year on the H1N1 influenza.

According to the Center for Disease Control and Prevention, as of November 13th, 2009, influenza activity was widespread in 46 States, almost all which was likely H1N1 influenza. There have been 22 million infections, 9,800 hospitalizations, and 3,900 deaths from the H1N1 virus, 540 of which have been confirmed pediatric deaths. This is a conservative figure, because not every child who dies from flu-related causes has been diagnosed with the flu. To date, there have been more pediatric deaths from the H1N1 than usually occurs in the entire annual flu season.

In September, Secretary Sebelius testified before the Energy and Commerce Committee indicating that by mid-October, the U.S. Department of Health and Human Services would be up and running with vaccines. In fact, CDC had projected that 40 million doses of H1N1 vaccine would be on hand by October 13th, but not even 13 million doses had arrived by October 22nd.

News reports have indicated that because of shortages in vaccines, doctors were dealing with worried and panicked parents who wished to have their children vaccinated while State and local health care departments are experiencing long lines that can

produce up to 5 hour waits for parents, children, pregnant women and seniors.

There have also been news reports indicating that private businesses, such as J.P. Morgan and Goldman Sachs, have been receiving the vaccines before individuals in the high risk category. And let's not forget about the reports citing military officials saying terrorists subjects being held at Guantanamo Bay would receive the vaccine before most Americans.

Like many districts around the country, my own district in northern Michigan has been affected by the H1N1 in a variety of ways. Since the outbreak began, Michigan has had over 500 schools shut down because 25 percent or more of their student bodies were absent with flu-like symptoms. Since September 1st, 1,226 people have been hospitalized in Michigan with flu-like symptoms, a 35 percent increase over last week, when 801 cases were reported.

The Oversight Investigation Subcommittee, along with the Health Subcommittee, have a responsibility not to merely rely on media accounts, but to get to the bottom of the situation. While we are not here to point fingers at who is to blame for the delay in the production and distribution of vaccines, we do need to shed some light on the process between the government and the manufacturers.

Given the urgency of the circumstances and the need for expeditious action, cooperation between drug manufacturers and Federal agencies is imperative to ensure that our country is prepared to respond to H1N1 and future pandemics.

When the H1N1 virus initially broke out, we knew very little, including how Americans would react to the vaccine, and if we would need more than one dose per individual. A vaccine didn't even exist. We did not know how different H1N1 vaccines were from the vaccinations for the seasonal flu.

In addition to discussion the specifics of H1N1 vaccine production and distribution, I hope we can shed some light today on our outdated vaccine process. It is my understanding that the manufacturing process for the H1N1 vaccine relies on obsolete egg-based influenza vaccine technologies that are subject to certain inherent uncertainties and delays such as incubation periods.

As a result, we will continue to face similar challenges in responding to future influenza outbreaks, both outbreaks of novel strains, such as the 2009 H1N1 strain and the pandemic or seasonal influenza we face every year. Many experts, including the CDC director Tom Frieden, have said that it is important to develop new technologies such as cell-based vaccine production.

We will hear from four of the five manufacturers that the U.S. Government has contracted with to produce and distribute H1N1 vaccines. These manufacturers will give us an in-depth knowledge of the production challenges that they face and share their thoughts on how we can improve this process as we move forward. GlaxoSmithKline was not invited to testify at the hearing as their vaccination was just recently approved by the FDA.

Joining the manufacturers is Dr. David Lakey, Commissioner of the Texas Department of State Health Services, who will be the voice of the State health departments across the country, and Dr. Jeffrey Levi, the Executive Director of Trust for America's Health,

a nonpartisan organization dedicated to making disease prevention a national priority.

I look forward to hearing from all of our witnesses today and delving deeper into the challenges that both the government and industry are facing with the H1N1 pandemic.

Thank you, Mr. Chairman. I yield back.

Mr. PALLONE. Thank you, Chairman Stupak.

The gentleman from Kentucky, Mr. Whitfield.

Mr. WHITFIELD. Thank you very much, Mr. Chairman. I suspect that every member of this panel has received many phone calls from their district, as I have, complaining about the shortage and wanting some answers and expressing their fear for their children and their family members.

As you said, we have had about three hearings on this subject matter, but today I really want to focus from my perspective on really the relationship and the interaction between the Federal Government, the State government and the manufacturers in the distribution process.

Number two, why have there been production delays specifically? Why? And why has there been difficulty in growing the virus? Is it because of technology? Is it because of process? Is it something else?

Then, third of all, I would like to touch on how does the U.S. compare in getting this vaccine out with other countries and how do our problems compare to those problems?

With that, I yield back the balance of my time.

Mr. PALLONE. Thank you.

The full committee chairman, Mr. Waxman.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you very much, Mr. Chairman. I want to thank you and Chairman Stupak for holding this joint subcommittee hearing on the H1N1 virus and how we are responding to it.

The reports on H1N1 are sobering. As of last week, 46 States are now battling the disease. CDC estimates that perhaps 22 million people have been infected with H1N1 and as many as 98,000 have been hospitalized and about 4,000 have died, including 540 children. This is a harsh reminder that we don't need a bio-terror attack or other man-made disaster to threaten our health and make us worry for our children.

In several ways, we have been well-prepared. The Federal and State governments have been preparing for a pandemic for several years. Our surveillance worked and we were able to catch the H1N1 relatively early in its spread. Federal and state governments have developed and exercised pandemic plans. Public education has been commendable.

There are five safe and effective FDA-approved H1N1 flu vaccines now available, and FDA has the authority for emergency use authorization to allow for unapproved but promising drugs and other products to be used to prevent and treat H1N1 flu. FDA has

used this authority to make antivirals, diagnostics and personal protective gear available in the fight against this flu.

But there are clear gaps in our preparedness. We had widespread disease before we had vaccines, and vaccine supplies have been more limited than we had hoped. At the same time, hospitals and other health care providers have been stretched to capacity.

We know that the best way to protect ourselves from the flu, H1N1 or seasonal flu, is to get vaccinated. Because of this, the Obama administration contracted to purchase 195 million doses of H1N1 vaccine. They also picked up the full cost to the States for purchasing the vaccine. The hope was that a robust vaccine supply would arrive before infections began to soar and everyone worked as quickly as possible to meet that goal.

These hopes were not met. The past several weeks have reminded us that the process of making flu vaccines is unpredictable and challenging. Millions of chicken eggs have to be injected with virus and then the virus has to grow. Unfortunately, this virus initially grew much more slowly than anticipated, and this lag has caused most of the delay in producing and delivering needed vaccine supplies.

There is understandable frustration in the face of a growing number of infections and long lines at vaccination clinics. Parents are understandably concerned about getting their children immunized as quickly as possible.

I want to make sure that everyone who needs the vaccine has access to it. At the same time, there have been unprecedented levels of collaboration among Federal agencies, the vaccine manufacturers and the States, and according to experts, the manufacturers' ability to produce a vaccine within 6 months after identifying the virus is impressive.

These efforts, while significant, are not enough for those people who are still seeking immunization. I look forward to today's testimony so we can understand where we are in the epidemic and the vaccine Nation effort. We also need to learn how the process can be improved. Both in the short-term so that people can be protected from this disease as quickly as possible, and in the long term, so that when we face the next flu pandemic, we can be even better prepared than we have been this year.

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

Mr. PALLONE. Thank you, Chairman Waxman.

Next we have the gentleman from Illinois, Mr. Shimkus.

OPENING STATEMENT OF HON. JOHN SHIMKUS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ILLINOIS

Mr. SHIMKUS. Thank you, Mr. Chairman. I too want to mention our sincere prayers for those who have lost family and loved ones during this illness. They are throughout the country, and I think a lot of districts have been affected.

Information has been good as far as there is more people washing their hands, there is more people covering their mouths, as Greg Walden mentioned, staying at home, and that is a thing where information has been very, very helpful. Information has

also been harmful, and that is this rush and this fear of people lining up for the injections or the mist sprays.

So my concern is we have got to be real about the projection of information to the public, because the public will respond appropriately. I think the rosy expectations have really caused this dilemma that we are in.

The other thing that I think we should focus on is this is something that we have had a year in essence to prepare for. What if, in our first thoughts about a pandemic after September 11th, is there is something we cannot prepare for, we do not know what has hit, and how do we ramp up, get information out, and then respond? I think that is as critical a question in the Homeland Security terrorist debate as responding to something we can prepare for.

So there are a lot of things we can learn about in the hearing today, and I appreciate the first panel and the follow-on panel. I think we will be very attentive to your testimony and I think there will be a lot of good questions offered by members.

I yield back my time, Mr. Chairman. Thank you.

Mr. PALLONE. Thank you, Mr. Shimkus.

Chairman Dingell.

OPENING STATEMENT OF HON. JOHN D. DINGELL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. DINGELL. Mr. Chairman, I thank you, and I want to commend you and Chairman Stupak for holding this hearing, which is very important.

Since the initial outbreak in March of the H1N1 influenza in Mexico, the Federal Government, State and local public health departments, health providers, vaccine manufacturers and many others who have been working overtime to produce and distribute the H1N1 vaccine and to educate the public on precautions that can be taken to prevent the spread of the influenza.

Since April, 42 people in Michigan have died since contracting any strain of influenza. More than 1,200 have been hospitalized and over 584,000 have reported flu-like symptoms. Across 48 States, there have been 3,900 deaths from H1N1 virus, 9,800 hospitalizations and 22 million infections. The high number of deaths from H1N1, in particular the high number of pediatric deaths has increased the demand for the vaccine, a demand that is unlikely to cease at any time soon.

This vaccine first became available in the beginning of October, and as of November 5, approximately 35 million doses have become available. This is well below the CDC prediction of 40 million doses by the end of October. There is no doubt that manufacturing a vaccine in short order is a difficult task and this country has had difficulties with flu vaccines before.

This task requires scientists to identify the virus correctly, determine the appropriate and most effective method for a vaccine, and then manufacture millions of vaccines to be distributed, all with the pressure of completing the task quickly and, most importantly, safely.

I know that there are many unforeseen roadblocks to manufacturers, whether it be the difficulty in producing the vaccines in an egg-based system, a shortage of appropriate egg supply and equipment, and equipment failures, amongst other things. While this shortfall is a disappointment, I believe we better serve the American people when we focus on producing a safe and effective vaccine and having it made available in a safe and efficient manner.

History has taught us that prioritizing speed over safety is shortsighted when it comes to flu outbreaks. In February of 1976, two recruits at Fort Dix fell sick from the H1N1 flu strand. Congress responded swiftly. That August, the National Influenza Program was produced and one week later was signed into law by President Ford. We were forced to deal with the costly consequences of our actions, which ultimately led to great public mistrust of immunizations as the program was mishandled and lives were lost.

It is appropriate to respond to the national threats, but we need to remember to be deliberate and thoughtful and wise in our response.

The H1N1 outbreak and the distribution of the vaccine provides the Federal Government with an opportunity and the responsibility to closely examine our pandemic response system. For HHS and CDC in particular, this means examining the way in which our government communicates with the public. For FDA, this means examining the methods in which the vaccines are approved.

For many of my colleagues and for many of those testifying today, my goal is to ensure the safety and health of the public, while at the same time looking forward to how we can best prepare for future pandemics and how we can learn from the ongoing events of the day.

This will include examining the national strategic stockpile and whether it is adequately supplied, preparing our scientists and manufacturers with the most effective and efficient technology to create and produce vaccines, as well as looking to whether or not the Congress has provided adequate funding for HHS, CDC and FDA to give them the resources needed to carry out their missions.

Today, I believe this hearing will be helpful in answering these questions and others, and I look forward very much, Mr. Chairman Pallone and Mr. Chairman Stupak, to working with you and hearing what our witnesses have to say today as we seek to mitigate the outbreak of H1N1.

Thank you, Mr. Chairman. I yield back the balance of my time.

Mr. PALLONE. Thank you, Chairman Dingell.

Next is the gentleman from Texas, Mr. Burgess.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Dr. BURGESS. Thank you, Mr. Chairman.

Like so many other Members of Congress on a Sunday afternoon in April, a football game was interrupted with a notice of a public health emergency about a new kind of flu. We had a conference call later that day for Members of Congress, I don't know how many were actually on the call, but I remember thinking at that time, our greatest danger here is not anticipating how aggressive this

virus could be if we are truly faced with the novel influenza for which most of us do not have preexisting immunity.

And that is sort of where we are today. Fortunately, the story is not nearly as bad as it could have been and many of us feared it might be, but nonetheless, it points up some of the difficulties that have been encountered.

Mr. Chairman, I will say I am grateful we have had three hearings, but it seems to me when we were preparing for a possible avian flu pandemic in 2004, 2005 and 2006, we had many more hearings for just the preparation for that possible pandemic than we have had after we find ourselves in the throes of this illness.

Now, we do have to ask ourselves, how could we have misanticipated the ability to produce vaccine? We saw this coming, we knew it was coming, we had reports over the summer from the southern hemisphere that it wasn't as bad as it could have been, and yet there were some particularly vulnerable populations which would need perhaps aggressive use of vaccination protocols, and we find ourselves in our districts without being able to provide even the vaccines for those high risk individuals.

In fairness, I do want to say I have had good cooperation from the CDC, the Department of Homeland Security, the Department of Health and Human Services, that came to my district in August and had a roundtable with school districts in my area so they could be better prepared. The Fort Worth Independent School District took a lot of heat last April and May for closing their school district early, but they were frightened of what might happen with not anticipating the severity of this illness.

Then just finally, on a personal note, I want to thank Dr. Lakey for being here from the Texas Department of Health. He has also been good enough to do conference calls with members of the Texas delegation as we worked our way through some of the difficulties with the distributional issues of getting the vaccine where it is needed.

I will also just thank Dr. Hamburg at the Food and Drug Administration, who was kind enough to take my call after the news reports said that Texas was getting expired Tamiflu to protect its citizens. And this was one of the problems we encountered in 2005. We produced a lot of anti-viral, the illness doesn't materialize, and how long is the shelf life? And, indeed, there were tests done to ensure that that shelf life was longer than what was stamped on the box. It was just an unfortunate public relations aspect that we didn't correct that. But I was very grateful to Dr. Hamburg for calling me and helping me through that particular public relations crisis.

Thank you, Mr. Chairman, for the consideration. I yield back the balance of my time.

Mr. PALLONE. Thank you, Mr. Burgess.

The gentlewoman from California, Ms. Eshoo.

OPENING STATEMENT OF HON. ANNA G. ESHOO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Ms. ESHOO. Thank you, Mr. Chairman, for holding this important joint hearing on H1N1 preparedness, production and distribu-

tion. I appreciate the witnesses being here today and I look forward to their testimony.

As we have heard from our constituents or experience in our own families, the H1N1 pandemic has proven to be widespread and really highly contagious. Since the vaccine was first slated for distribution in mid-October, I, along with, I am sure probably all of my colleagues, have received countless calls from constituents asking when they can get the vaccine. Lines of patients have been out the door and around the block, and the news has been filled with stories of empty clinics and angry parents.

While I don't think there is one source to point out relative to production and distribution problems, I am interested in looking at the systemic reasons for the somewhat antiquated vaccine process we have today.

For more than half a century, the United States has been using egg-based technology to create vaccines. While it is safe and effective, it is a slow-moving process. Across Europe, vaccine developers are using the faster process of incorporating mammalian cells to grow vaccine. As we begin to explore cell-based technology, I would pose the question, will there be an adequate FDA approval process for these new vaccines?

I am also interested in hearing from the vaccine manufacturers on how they ramped up production, in some cases to ten times their normal production schedule. We know that production has been delayed for H1N1, a harmful but relatively moderate virus, compared to something more lethal like the Spanish flu. But in the case of a stronger virus with a higher fatality rate, would our country be able to produce enough vaccine for everyone in a short time period?

So I look forward to questioning the witnesses. I welcome them again, and learning more about how we can improve vaccine production in our country. And, again, I thank the chairmen for this joint and important hearing.

I yield back.

Mr. PALLONE. Thank you, Ms. Eshoo.

The gentleman from Pennsylvania, Mr. Murphy.

OPENING STATEMENT OF HON. TIM MURPHY, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. MURPHY OF PENNSYLVANIA. Thank you, Mr. Chairman.

As we look at how we are handling this latest crisis in our government, I reflect back on a few years ago when we were faced with the sudden and unanticipated problem of Hurricane Katrina which led to an unfortunate between 1,300 and 1,800 lives lost from the hurricane and the flood itself. But it also resulted in a flood of Members of Congress repeatedly and bitterly attacking the administration and anybody else in town because of the government's mismanagement of the whole issue.

Now, of course, it begs the question, who do we blame this time for where we are, or should we stop that game and simply get down to the business of understanding we want a painfully candid and brutally honest assessment of what is happening, what has gone right, what has gone wrong, do we have any weaknesses, and

what do we need to do about it. I would hope it is this case instead, that we use this hearing as an opportunity to be honest with each other.

We are all deeply concerned of the thousands who have lost lives, the thousands who have been hospitalized, and, quite frankly, the millions who are worried that they might be affected by this latest virus hitting our Nation.

We recognize the incredible scientific achievements, and quite frankly, I would like to compliment the manufacturers for working so hard in trying to develop the vaccines and the nasal systems for sending out these things to help us deal with this virus.

But we still have a long way to go, and we are having this hearing today, quite frankly, because we are concerned. Something is not going right. Was it the goals were set too high, too unrealistic? Was it done somehow to assuage the worries of the public about something we were not ready to do, or can we really meet those goals?

I am looking forward to hearing from all the witnesses today. We have a very talented panel before us. I am excited to hear what you have to say. But more than anything else, let's use this as an opportunity to be honest, not political, and really work for some solutions.

I yield back my time.

Mr. PALLONE. Thank you.

The gentleman from Texas, Mr. Green.

OPENING STATEMENT OF HON. GENE GREEN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. GREEN. Thank you, Mr. Chairman. I want to thank you for holding this hearing today and giving us an update on H1N1 vaccine production and distribution.

Texas has ordered its full allocation of 3 million doses of the vaccine, but that order has not been filled due to the slow production and supply of the vaccines. I worry that States like Texas, which is the second largest State, whether they are receiving their fair share of these vaccinations. We are a border State and with that comes a great deal of border issues, along with swift transmission of infectious diseases.

I welcome Dr. Lakey, who is the Commissioner of the Texas Department of State Health Services, who will be testifying on our second panel today. He assured me that Texas is receiving its fair share of vaccines and the State is continuing to order of the maximum the amount. The issue is whether the commitments of production are being met and why they are not.

I would like to highlight a piece of legislation I sponsored along with our colleague Representative Tim Murphy, H.R. 2596, the No Child Left Unimmunized Against Influenza Act. The bill would allow HHS to perform a voluntary multistate demonstration project to test the feasibility of using the Nation's elementary schools and secondary schools as influenza vaccination centers in coordination with school nurses, school health programs, local health departments, community health care providers, State insurance agencies and private insurers.

I am pleased the bill was included in H.R. 3962, the Affordable Health Care For America Act, that was passed out of the House. Schools are logical places to vaccinate our children. Parents can opt into the program and not have to take time off from work to get their child vaccinated, which in a blue collar district like ours is hard to do.

Again, the issue is why haven't the production goals been met? Did we fill the requests from the various States?

I thank our witnesses who are here today. It appears we will know what problems have occurred with H1N1 vaccination production and distribution and how we can fix it, and I hope we will learn from the mistakes and hopefully make it much better.

I yield back my time.

Mr. PALLONE. Thank you.

The gentleman from Missouri, Mr. Blunt.

OPENING STATEMENT OF HON. ROY BLUNT, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MISSOURI

Mr. BLUNT. Thank you, Mr. Chairman, and thank you Chairman Stupak for holding this hearing.

This is an important topic, obviously, and one we ought to be concerned about. I have been concerned about both the vaccine distribution process and, frankly, the misleading overestimates of vaccine availability. I believe Mr. Waxman, the Chairman of the full committee, said in his statement that the administration's hopes were not met. Well, apparently hope does not get the job done here.

In addition to their hopes not being met, I think it is outrageous that suspected terrorists at Guantanamo Bay and Wall Street people, people who work on Wall Street, were apparently slated for access to the vaccine ahead of the people that health care professionals said were in danger.

Since October, 43 million vaccines have been made available, but that falls far short of the 159 million people considered to be at high risk because of these complications. It also falls short of the government's original projection that 120 million vaccines would be available by mid-October.

In fact, just last week, the government was still estimating that 8 million vaccines were going to be shipped, when only 5 million were released. I don't know how we could be this far into this process and still be 40 percent off in our one week estimate. So I will be interested to hear the answers to those questions.

In Missouri alone, there have been 60 school closings this year since the beginning of the year. Last year, during the same period, there were none. Since October 4th, approximately 21,700 people in Missouri have possible cases of H1N1 flu. During the first 6 months of last year's flu season, there were 28 cases of all kinds of flu. Sadly, last week in Missouri, the eighth person died from complications with H1N1.

I want to know and the people I work for want to know where this problem came about, the failure to understand the problem, to recognize the problem, to move forward with the problem; and with vaccine delivery, how long ago did we know that the vaccines were not going to be available and what could we have done about it?

Mr. Chairman, I expect some of those questions to be answered today, and I am grateful to you for holding this hearing.

Mr. PALLONE. Thank you, Mr. Blunt.

The gentleman from Pennsylvania, Mr. Doyle.

OPENING STATEMENT OF HON. MICHAEL F. DOYLE, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. DOYLE. Thank you, Mr. Chairman. I want to thank you for holding this hearing on the issue of H1N1 preparedness at such a relevant time.

As the Centers for Disease Control have recently reported, the H1N1 strain has now claimed over 4,000 lives since April of this year. Of those, over 500 were children. I am very sad to report that just this past week, a newborn baby died at Children's Hospital of Pittsburgh located in my district of suspected H1N1 influenza. If confirmed as being an H1N1 death, this will be the first reported infant death.

In the State of Pennsylvania alone, 9,600 cases have been reported. Nearly 1,800 of them have been in my Congressional District. This is indeed a very serious problem.

This pandemic is different than what we are used to dealing with every fall as the target is an unlikely and unusual population. This strain is mostly affecting younger people, with more than 70 percent of the reported cases in Pennsylvania involving people under the age of 25. Antivirals are playing an increasingly important role in fighting this epidemic, and I am happy that the FDA has recognized this by issuing emergency use authorization for intravenous administration of these potentially lifesaving drugs.

I do have serious concerns about the reports of the difficulty doctors have had in obtaining enough vaccines for their patients, and I am anxious to hear our witnesses testify to this. This year's distribution plan for the vaccine was unprecedented, and I am extremely interested in the opinions of our panel of its effectiveness. I think that this hearing will serve as an important venue to hear from all sides of this issue and help us all work together so that in the future, we know what works and we know what must be improved upon.

I look forward to hearing from our witnesses, and I want to thank you all for your testimony today. Again, I want to thank the committee for holding this important briefing.

I yield back.

Mr. PALLONE. Thank you.

The gentlewoman from Tennessee, Ms. Blackburn.

OPENING STATEMENT OF HON. MARSHA BLACKBURN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TENNESSEE

Ms. BLACKBURN. Thank you, Mr. Chairman, and I want to say thank you to each of you for taking your time to prepare and to come and to be in front of us. We do appreciate it.

I join other members on this panel in extending our sympathies to those who have lost life or who have found a serious complication to their health through this process.

I bring a perspective of being a grandmother and also a good friend to lots of school teachers that have kept me informed of what is happening on this. As a grandmom, I have a daughter who has an 18 month old and a 5 month old, and I know the "mommy blogs" have just been filled with the frustration of young mothers trying to get to this vaccine. It has been like playing "Where's Waldo" trying to find who has it.

We have done a disservice to these young mothers because you all knew this was coming, appropriate preparations were not made, and these are some of the questions we are going to want to get to today.

I want to talk with you about the delays and what you think has caused those, the communications processes, and where the breakdowns have been between you all and HHS, because we had different messages that were coming out. That is confusing to the public. I think also the processes that were in place for approval, for distribution, and then certainly looking at the diagnosis-confirmation portion of that.

Then let's talk about lessons learned and how we moved forward. Dr. Schuchat, I pulled a Reuters article, a comment you made in here where you say "I think the key barrier to our immunization effort is really the fragility of the public health infrastructure."

I would love to explore that comment with you. Thank you all. Thank you, Mr. Chairman. I yield back.

Mr. PALLONE. Thank you.

The gentlewoman from California, Ms. Harman.

OPENING STATEMENT OF HON. JANE HARMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Ms. HARMAN. Thank you, Mr. Chairman. So far, there have been 3,900 deaths in the U.S. from the H1N1 flu, with 266 deaths in California. This compares favorably, it is less than annual deaths that are expected from the seasonal flu. I suppose that is good news. But I agree with Chairman Waxman that this is our rehearsal for a major terror attack from some sort of biological weapon, and I think our grades are very mixed.

In terms of preparing the public, I think we have done very well, and I commend the panel and I commend others in our Federal Government for making the case calmly and providing lots of details for what the public is supposed to do. I would give that an A.

In terms of preparing the vaccine, we have had a lot of mixed results, and I suppose that could be a B-minus.

But in terms of distributing the vaccine, I would give us a D-minus. A lot of that is the lack of preparation to States and localities for exactly what they should do with scarce resources.

I was personally scared because I have a pregnant daughter-in-law who had to spend weeks in New York City finding a doctor who had the vaccine. She did get vaccinated.

But in my district, the Beach City Health District, one of the first providers able to offer the vaccine, had a drive-in event recently. People drove more than 100 miles from as far as Santa Barbara and San Diego, turning what was supposed to be a local event into a regional scramble. The line of cars leading to the clinic

backed up for miles, police were deployed to manage the unexpected crowds, and all this mayhem was just for 3,000 doses of vaccine. It was a disaster and now other areas are not doing the same thing.

As my time expires, the distribution piece was a failure, and I hope our witnesses have learned from this and they will move forward much more effectively.

Thank you, Mr. Chairman.

Mr. PALLONE. Thank you, Ms. Harman.

The gentleman from Georgia, Mr. Gingrey.

OPENING STATEMENT OF HON. PHIL GINGREY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Dr. GINGREY. Thank you, Mr. Chairman. Today, the Subcommittee on Health and the Subcommittee on Oversight and Investigations will have an important opportunity to shed some light on our government at work and what is a matter of life and death, and hopefully we will be able to gain a few answers to the many questions our constituents have asked us about H1N1 preparedness and the Obama administration's response.

Mr. Chairman, from fiscal year 2004 to 2009, this Congress appropriated almost $7 billion for pandemic flu preparation. Congress also provided an additional $6.4 billion in the fiscal year 2009 supplemental, bringing the total since fiscal year 2004 for pandemic flu preparation to almost $13.4 billion.

Without question, the promotion of the public health and safeguarding the lives of all Americans is an important national priority. But we also have a solemn duty to thoroughly scrutinize every dime we appropriate, because every single dime is one more IOU that will be thrown upon the backs of our children and grandchildren, likely for decades to come. Both the American people's physical health and fiscal health have to be priorities for this Congress.

Mr. Chairman, I make this point because I have concerns about this government's response to H1N1, and I believe that it may be a microcosm of what is in store if the health care legislation this House passed 10 days ago becomes law. When this government prioritizes KSM, Khalid Sheikh Mohammed to receive a vaccine, when this government has enough vaccine for Guantanamo Bay but not for Grandma Kay, we have a big problem. Is this what the American people expected? Is this what the American people deserve? At the same time, this Congress continues to put them and their children further and further into debt.

Mr. Chairman, I think not. I hope that today we will be able to pull back the curtain for the American people so they can see how the government attempts to manage their health and their collective pocketbook.

I yield back.

Mr. PALLONE. Thank you.

The gentleman from Arkansas, Mr. Ross.

OPENING STATEMENT OF HON. MIKE ROSS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ARKANSAS

Mr. ROSS. Thank you, Mr. Chairman. I would like to thank the Chairman and ranking member for having the Energy and Commerce Committee hold today's hearing on H1N1 preparedness.

Over the course of this year, we have seen the strain of influenza spread to a global proportion and lead to a declaration of national emergency. According to the CDC, as of November 13, 2009, influenza activity was widespread in 48 States, almost all of which is likely H1N1 influenza. Furthermore, there have been 9,800 hospitalizations, 22 million infections and 3,900 deaths from the H1N1 virus, 540 of which have been confirmed pediatric deaths.

Both public and private sectors have attempted to work together in an expedited effort to ensure adequate vaccine production and delivery to patients. Unfortunately, such efforts have fallen short and we have seen major delays in access to this much-needed vaccine. As a result, we have thousands of individuals, including those in high-risk categories, still waiting for the vaccine as we fight this pandemic.

I am also deeply concerned about the impact of H1N1 on our children and our schools. During seasonal flu outbreaks, 95 percent of deaths are usually among those older than 65, but for the swine flu, 95 percent of the deaths are occurring in those younger than 65, and typically among those far younger than that. My concern is that every parent who wants to get their child vaccinated should have the opportunity to do so. The delays in getting the vaccine to the American people must be addressed and fixed now.

Clearly there are problems with the current process in place that could have been prevented. The public deserves answers as to why there is such a shortage in supply of a vaccine when H1N1 has posed such a serious health threat for months.

I look forward to hearing answers to these and other related questions.

With that, Mr. Chairman, I yield back.

Mr. PALLONE. Thank you.

The gentleman from Pennsylvania, Mr. Pitts.

OPENING STATEMENT OF HON. JOSEPH R. PITTS, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. PITTS. Thank you, Mr. Chairman, and thank you Chairman Stupak for convening this joint hearing.

I am sure that all of us have received phone calls and e-mails from anxious parents wondering if they will be able to obtain the H1N1 vaccine for their children. I am sure we have all been stopped by constituents back home wondering when the vaccine will be available in their area and worried that there is a shortage.

Today we will hear from the government departments and agencies tasked with responding to the H1N1 pandemic and from the manufacturers of the vaccine itself to determine how much vaccine has been produced and how much more is on the way and how it is being distributed and allocated. I also anticipate that we will suggestions for how production and distribution could occur more smoothly in the future.

On our second panel, I would like to specifically welcome Phil Hosbach, Associate Vice President of Immunization Policy and Government Relations, the head of the Sanofi Pasteur global influenza pandemic crisis team. The U.S. headquarters for Sanofi Pasteur is in my home State of Pennsylvania. The Pennsylvania site is also the only domestic manufacturing sight of injectable flu vaccine, and the employees there have been working around the clock to produce both seasonal and H1N1 influenza vaccines.

I would also like to welcome Paul Perreault, President of CSL Biotherapies, which has its headquarters in King of Prussia, Pennsylvania, right outside my district.

Mr. Chairman, again, I thank you. I look forward to hearing the testimony of all of our witnesses, and I yield back my time.

Mr. PALLONE. Thank you.

The gentlewoman from Wisconsin, Ms. Baldwin.

OPENING STATEMENT OF HON. TAMMY BALDWIN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF WISCONSIN

Ms. BALDWIN. Thank you, Mr. Chairman, for holding this very important hearing.

I want to highlight three issues that I hope our witnesses will address according to their expertise during our hearing this morning.

Clearly a thorough response to any public health emergency such as a flu epidemic requires a partnership between local, State and Federal public health agencies and labs, and I am concerned about resource shortages at the State and local level, particularly with regard to personnel and modern information technology and communications. I have a bill on that matter and would like to hear your insights on how those resource shortages have affected our response to this flu, H1N1.

Secondly, I would like an update on the State of innovations and improvements that many of my colleagues have referenced that will help us do a better job next time. Cell-based manufacturing technologies, the use of adjuvants and alternative methods of vaccine delivery beyond injection or nasal sprays.

Lastly, and I think most importantly to me, I would like the witnesses' comments on our lack of domestic manufacturing of H1N1 and seasonal flu vaccine. This is of great concern to me, and I asked this of our Secretary of Health and Human Services when she last appeared before the committee. It appears that we have five contracts with five manufacturers for H1N1 vaccine. Only one does its bulk manufacturing in the United States, in the State of Pennsylvania.

I think that if we were to ever face much greater flu that presents much greater virulence, it would be a question mark whether we would be able to get supplies of vaccine from production sites in other countries. Any country that hosts vaccine manufacturers would want to assure that their own population was protected first before permitting the export. So I am very concerned about the lack of domestic manufacturing presence and would like your comments on that.

I yield back.

Mr. PALLONE. Thank you.
The gentleman from Oklahoma, Mr. Sullivan.

OPENING STATEMENT OF HON. JOHN SULLIVAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF OKLAHOMA

Mr. SULLIVAN. Thank you, Mr. Chairman. Thank you for holding this joint hearing today on the national H1N1 swine flu preparations, especially on the current status of the vaccine production and distribution. I am interested today in examining the lessons learned from both the administration and vaccine manufacturers in terms of responding to this national public health emergency.

To date, manufacturers have delivered 48.5 million doses of H1N1 vaccine, and the Department of Health and Human Services had hoped to have as many as 120 million doses by now. Obviously there is a large gap between what the administration promised and what they were able to coordinate and deliver. I am concerned that the administration's plan was overly optimistic and that this has led to confusion with the American public.

Since September 1, 890 Oklahomans have been hospitalized due to complications from influenza and 27 persons have died. Ninety percent of the H1N1 related deaths have been persons less than 65 years old.

Health officials in my State announced yesterday that all Oklahomans who wants to reduce the risk of H1N1 infection are now eligible to receive H1N1 influenza vaccine. While vaccine supplies are limited, demand from priority groups has dipped to a point where all Oklahomans can begin to receive vaccine. H1N1 influenza activity has been widespread in Oklahoma since early September, and even though statewide monitoring has recently shown a decline in influenza linked to hospitalizations, this virus is expected to circulate throughout the winter months. The possibility also exists that another surge of H1N1 flu may follow the current one and we need to be prepared for this contingency.

I look forward to hearing the testimony of our witnesses today and examining how we can continue responding to this public health emergency, and I yield back the balance of my time.

Mr. PALLONE. Thank you. The gentlewoman from Florida, Ms. Castor.

OPENING STATEMENT OF HON. KATHY CASTOR, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

Ms. CASTOR. Well, thank you, Chairman Pallone, and good morning to our witnesses. The CDC and Secretary Sebelius and all of you have done exceptionally well in your public health outreach. You have kept Americans informed about the risk in basic prevention methods to combat the spread of the virus such as hand washing and the use of alcohol-based sanitizers. And I appreciate Secretary Sebelius' visit to Florida last week. She visited the East Manatee Family Health Care Center in Bradenton, Florida. And we met personally with representatives from the health department, community health centers, and other providers throughout the area to review local distribution of the vaccine, particularly to

people in the high risk categories like pregnant women and young children and others with asthma and diabetes.

My greatest concern right now is the spread of misinformation, especially on the Internet. Just over the past weekend I was talking with a doctor who I know who is also—who works in Tampa General Hospital. He is married to an OB/GYN. And they were explaining to me that they are running into the problem of pregnant women and others in high risk categories that have read something on the Internet that has discouraged them from receiving the vaccine. And after talking with them I went online to see what is out there, and they are right, there is a lot of misinformation on the Internet.

One Web site calls it a complete load of nonsense, that mainstream media and American public health officials state that the benefits of H1N1 vaccine far outweigh the risks. They are frightening pregnant women who are at high risk to think that they might miscarry if they are vaccinated. This Web site reports that the vaccine is responsible for death, paralysis, seizures and other ailments.

So we have got our work cut out for us. But it doesn't stop there. In September a major cable news network did a segment with a so-called infectious disease expert advising parents not to vaccinate their children and declared that he would not vaccinate his own children, claiming that the vaccine and others are not safe and they cause more serious devastating conditions.

So in your testimony would you please address how we can effectively combat the spread of misinformation and continue to empower communities with accurate information and continue to encourage those, especially in the high risk categories, to receive the vaccination.

Thank you. I yield back.

Mr. PALLONE. Thank you. The gentlewoman from Illinois, Ms. Schakowsky.

OPENING STATEMENT OF HON. JANICE D. SCHAKOWSKY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ILLINOIS

Ms. SCHAKOWSKY. Thank you, Chairmen Pallone and Stupak.

I wanted to put on the record the effective manner in which my State of Illinois is handling the H1N1 flu vaccine and administration. The Illinois Department of Public Health has an H1N1 specific Web site that contains a wealth of information about vaccine availability and prevention information.

The City of Chicago set up six free clinics to administer H1N1 vaccines at city colleges. Chicago vaccinated nearly 51,000 people in the 7 days following the opening of the free clinics.

There are a number of issues surrounding the infection and death rates in Illinois that lack sufficient explanation. Maybe you have these answers. Why is the highest number of H1N1 deaths among adults age 25 to 29? These numbers defy all the things that we previously knew about flu viruses. Do we have the correct distribution system? Is giving the vaccine to banks and companies likes Goldman Sachs and NBC the best way to distribute the vaccine?

Our current lack of research data limits our ability to draw concrete conclusions, and if we are unable to draw conclusions there is no way we could construct an adequate or effective response plan which only increases all of our risk.

So I hope to hear about the public health plans and research efforts under way to help us better understand the disease and innovation prevention and treatment methods that are emerging.

I thank all of the witnesses for being here today to help shed more light on the situation, particularly as we are learning new information every day, and I look forward to your testimony.

I will yield back.

Mr. PALLONE. Thank you. The gentleman from Utah, Mr. Matheson.

OPENING STATEMENT OF HON. JIM MATHESON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF UTAH

Mr. MATHESON. Well, I want to thank both Chairmen Stupak and Pallone for holding this hearing today. My State is not unlike my colleagues here on the committee. We have had our outbreaks of H1N1 in schools and communities. We have seen over 623 hospitalizations due to the influenza this year as well as 14 deaths. Our State has worked with the Federal Government and manufacturers to make as many vaccines available as possible to our residents, and I am looking forward to hearing how we can better improve our strategy and coordination for responding to this public health crisis.

To date my State of Utah has received a total of just over 296,000 doses, and providers have reported having administered just over 176,000 doses of the vaccine as of November 7th. While our State supply of vaccine continues to arrive in weekly shipments, the vaccine is still in limited supply.

I represent the State with the youngest population in the country. So I continue to be worried about making sure our children get access to this vaccine in a timely fashion. I am also concerned by several recent reports in the uptick of counterfeit medications.

The U.S. Food and Drug Administration has issued warnings to consumers to use extreme care when purchasing products over the Internet that claim to diagnose, prevent, treat, or cure the H1N1 influenza virus. The agency issued this warning after the FDA recently purchased and analyzed several products represented online as Tamiflu.

The FDA notes on its Web site that one of the orders which arrived in an unmarked envelope with a postmark from India consisted of unlabeled white tablets taped between two pieces of paper. When analyzed by the FDA the tablets were found to contain talc and acetaminophen but none of the active ingredient.

I am working on legislation to proactively address the rise in counterfeit medications with my colleague, Mr. Buyer. Counterfeiting is a lucrative business, and I hope that my colleagues will proactively work with me to address this issue with any drug safety legislation to come before this committee.

Thank you, Mr. Chairman. I yield back the balance of my time.

The CHAIRMAN. Thank you. The gentleman from Ohio, Mr. Space.

OPENING STATEMENT OF HON. ZACHARY T. SPACE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF OHIO

Mr. SPACE. Thank you, Mr. Chairman, for conducting this important hearing. We have heard today already a couple of allusions to Guantanamo Bay and I think one to even Katrina. And I am as concerned as anybody about the specter of Khalid Sheikh Mohammed getting this vaccine before my son. And I guess I would like your assessment as to whether that is in fact happening.

But more importantly, I think it is important that we understand what we can do as a legislative body at this point to enhance our ability to manufacture and distribute the vaccine in a better way. We have obviously seen far too many deaths across the country. Certainly Ohio and my congressional district has been no exception to that.

But I am also interested in hearing your opinions concerning other ways that we can combat this H1N1 pandemic apart from administering the vaccine. My colleague from Florida referenced the misinformation campaign that seems to be occurring out there. I am curious as to the educational component that we can promote in simple things like hand washing and things that our constituents can do to put themselves in a better position.

And finally your assessment as to those who are most likely to get sick and die if they contract the virus, what they can do. In particular, diabetes. I understand that the obese have a particular risk factor. And how we can again from a legislative perspective at this point in time do everything we can to maximize our ability to combat this troubling epidemic.

Thank you, and I yield back my time.

Mr. PALLONE. Thank you. The gentlelady from Ohio, Ms. Sutton.

OPENING STATEMENT OF HON. BETTY SUTTON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF OHIO

Ms. SUTTON. Thank you, Mr. Chairman, and I appreciate you holding this hearing today. So much has changed since this committee held its first hearing on H1N1 back in April. At that time the H1N1 flu was just breaking and there were only 91 confirmed cases in the U.S., including a young boy in my district. There was also no vaccine and the government was just beginning to formulate a Federal response to the growing pandemic.

So we have traveled some distance since then. Now nearly 8 months later over 22 million Americans have had the H1N1 flu, and there is a vaccine in production, as we all know, and it is being distributed free of charge to the American people. However, there have been challenges along the way, and we have heard that discussed here today, with manufacturing and distribution of the vaccine. And because of the slow rate of vaccine production, demand has outpaced supply and the vaccine remains difficult for people to obtain. It is difficult even for those in high risk populations sometimes.

So it is very important that we have this hearing and we figure out ways to address these challenges that we are facing currently and the ones that may be ahead. We have seen moms with young children and pregnant women and the elderly standing in lines hoping to get the vaccine, and we want them to get it. We have

heard the reports of Wall Street employees having access to the vaccine. And it certainly undercuts the public's confidence in the distribution process, which is important. And it is important that we correct the record so that people understand what is and isn't happening.

But it is also just critically important that we do everything we can to effectively deal with H1N1 from this point forward, and frankly this won't be the last flu challenge that we have, so that we can formulate the proper way to respond to these kinds of challenges in the future.

I yield back.

Mr. PALLONE. Thank you. The gentleman from Indiana, Mr. Buyer.

Mr. BUYER. I pass.

Mr. PALLONE. The gentlewoman from Colorado, Ms. DeGette.

OPENING STATEMENT OF HON. DIANA DEGETTE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF COLORADO

Ms. DEGETTE. Thank you very much, Mr. Chairman. I want to thank both of our chairmen for having this hearing today. I will submit my statement for the record because I am sure every single thing I had in there has been said by other members of the committee. But let me just say this.

The Oversight and Investigations Committee has had a number of hearings over the years on flu pandemics. The good news about what has happened with this pandemic is our public campaign, our awareness has been terrific, as Congresswoman Harman said. The problem is we still do not have an alternative to the egg-based vaccines, and we were assured at the September 15th hearing that we had that, we were ramping up production, we knew H1N1 was coming and those vaccines would be readily available very, very soon.

That obviously has been the big problem with our response to this pandemic. Now, it is not so bad because as it has turned out this particular strain, while fatal and we feel badly about the fatalities that we have had, is not as virulent as say the avian flu. But I will tell you what, if this had been a virulent flu strain like the avian flu we would have millions of casualties already.

Now, my own daughter, who is a Type I diabetic, spent weeks going around Denver trying to get a vaccine only to finally get it last week. And I have got to say over the 13 years I have been on this committee we have got to fix this problem. We can't wait until we have the next pandemic to say that we have got to get an alternative to egg-based vaccines.

And so again to both of our chairman I want to thank you for having this hearing. And I want to say that at least this Member of Congress intends to keep pushing even when this is out of the headlines to make sure we find these alternatives, because if we don't it will be on our shoulders the next time we have a pandemic and it is a virulent pandemic that causes millions of deaths.

So I intend to do everything I can to make sure that that will not happen the next time.

[The prepared statement of Ms. DeGette follows:]

November 18, Flu Hearing: Vaccine Production Distribution

Opening Statement

Mr. Chairman—I want to thank you for keeping this Committee's attention focused on the current H1N1 pandemic. It is imperative that we investigate all facets of this outbreak so that improvements in biosecurity preparedness and response are adopted. I also want to thank our witnesses for sharing their time today.

Influenza pandemics are not "if" phenomena, they are "when" phenomena, owing to the virus's ability to mutate. It is estimated that 10 influenza pandemics have transpired in the past 300 years. We are enduring the first pandemic of the 21st century, our fourth in the past 100 years, and certainly not our last.

While I believe we can do better to protect ourselves from influenza, I do want to commend progress in cooperation and communication amongst executive agencies, various levels of government, and the private sector. I am also pleased with the frequent updates on influenza epidemiology, vaccine production, and guidelines.

That being said, we can and must do better in terms of vaccine production and distribution. The vaccine shortage is **not** okay. New CDC estimates reveal approximately 22 million U.S. H1N1 infections mostly in young persons, 3,900 total deaths, and 590 pediatric deaths. Moreover, 8% of the U.S. population has asthma and yet asthmatics account for 32% of H1N1 hospitalizations.

One in four infected and hospitalized diabetics have required intensive care attention. In my district, Denver, Colorado, four weeks passed before a young girl with type 1 diabetes finally located H1N1 vaccine. Upon her arrival at the hospital, she discovered that her condition rendered her ineligible for the intranasal vaccine being administered, forcing her to wait yet another week to become immunized.

Despite all of this, we are in some ways fortunate with the current outbreak. Should this have been a reassortment strain with the severity of the endemic avian H5N1 strain, we would be facing a 60 plus percent fatality rate.

While I appreciate the long-standing establishment and optimization of egg-based vaccine production, by now we should be using newer technologies such as cell-based production, reverse genetics, subunit and virus-like particle vaccines, and others.

I look forward to hearing about vaccine innovations and what we in Congress can do to assist in your efforts, so that we are better prepared for the next influenza epidemic.

Mr. PALLONE. I thank the gentlewoman. Next is the gentleman from Connecticut, Mr. Murphy.

OPENING STATEMENT OF HON. CHRISTOPHER S. MURPHY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CONNECTICUT

Mr. MURPHY OF CONNECTICUT. Thank you very much, Mr. Chairman. To Chairman Pallone and Stupak, I appreciate this hearing today. I appreciate it especially as a parent of a current 15-month-old H1N1 patient at home. He is doing fine, but I am looking forward to the testimony today. For a number of reasons. One, I think that this conversation about how our Federal Government is interacting with State governments is important, and I know you are going to spend some time talking about how you turn your recommendations for distribution systems into best practices.

But I would also like to hear about your interactions with States regarding preventative measures. We have had a number of long-term school closures in Connecticut due to outbreaks, and I think one of the difficult things for local school districts has been an inability to really get the best information regarding how they should approach small or larger size outbreaks in school systems, in day care settings, and so I think a lot of us would be interested in hearing about how you are disseminating those recommendations down to school districts and to other settings in which you have a lot of kids.

And second, just to partner and build on the remarks of Representative Baldwin and Representative DeGette, I think a lot of us are very interested in the progress we are making this season, but also for next season, on alternative processes. I know that HHS has already given out some fairly large research grants to companies, one actually located in my district, Protein Sciences, to start building some nonegg-based processes that have I think some real potential, and I am interested in whether you think any of those processes might come online this season or whether we are looking out into the next outbreak or to the next season for some of these alternative processes.

But again I think there are a lot of questions but I think that you have answered many of them so far. I think you have done a great job in disseminating information and getting information out to the public, and I think that this hearing can just help you build on that.

I yield back.

Mr. PALLONE. The gentlewoman from the Virgin Islands, Mrs. Christensen.

OPENING STATEMENT OF HON. DONNA M. CHRISTENSEN, A REPRESENTATIVE IN CONGRESS FROM THE VIRGIN ISLANDS

Mrs. CHRISTENSEN. Thank you, Mr. Chairman, and I thank all of the Chairs and the ranking members for having this hearing. As a physician and a former public health administrator, you can imagine this issue is of great concern. And as someone who has managed emergencies in the past, I know how important communication is and managing them and controlling panic and controlling the spread of the disease in this case.

Since the spring, when we were first made aware of the H1N1, it is now widespread I think in 48 States and at least two Territories. As of the last report there are 80 cases in the Virgin Islands, I am sure there are more now, and one death. And 444 cases and 34 deaths in Puerto Rico. And I am very concerned that half of the children that died from H1N1 between April and August were African American and Hispanic children, which is considerably more than the percentage that both groups represent in the population. So I would like to hear something of what is being done to outreach to those communities, as I have asked before.

I want to say that several years ago I introduced the Rapid Cures Act, which would increase research to shorten the time from bug to drug and vaccine. I didn't introduce it in this Congress because I was assured that the research was being done and I thought we would be further along. But the shortage shows that we are probably not, and I am hoping also that the limitations that we have faced in providing adequate vaccine will allow real valuable lessons going forward, and I look forward to the testimony of our witnesses.

Mr. PALLONE. Thank you. Mr. Weiner.

OPENING STATEMENT OF HON. ANTHONY D. WEINER, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW YORK

Mr. WEINER. Thank you, Mr. Chairman. Mr. Chairman, I want to thank the members of the panel both for their work and for being here today. I represent the community around Saint Francis Prep, which represents I guess the closest thing to the American Ground Zero for this virus. You know frankly we have—this is the problem with trying to deal with a complicated health thing in the context of 24-hour news. And a lot of people who look at this through the lens of their own experience, we have swung wildly from poll to poll between this as an enormous problem that is going to smite us all to this is not that big a deal. We have the very same people who have been traveling the country saying get government out of our health care are now saying how come government isn't doing a better job with our health care.

I certainly hope that you have had a strong and stern talking to to those viruses that refuse to grow fast enough. I hope that any of those viruses that haven't been performing have been summarily dismissed. And I look forward to an oversight report by the GAO about how it is that we are recruiting a virus that does such a poor job of growing in chicken eggs when we ask it to.

But the bottom line of all of this is to some degree we have all participated in a small way to dealing with this notion of frenzy around this. Even the Vice President of the United States I think probably regrets saying he would recommend his family members not get on a subway in New York City, where you can catch things, but I am not sure swine flu is going to be at the top of your list.

The point is that we to some degree in government, we too exaggerate our ability sometimes to be able to be a fulcrum against Mother Nature and the laws of medicine and to some degree chemistry and physics and the like. And I think that you should be commended for trying to keep a level conversation tone here even in

the face of many different cross currents. We should try to learn each time we have one of these instances what we can do better. And I think to some degree a lot of what you have done now is based on lessons that have been learned.

But I think that it is also important that we as the legislative branch empower you all to do the jobs you can and then do our best to give you the elbow room to try to make smart medical decisions in what is an environment that is often hypertense, hypersensitive, and often polluted with a lot of misinformation.

So I appreciate your being here to help us do that.

Mr. PALLONE. Thank you. The gentleman from Georgia, Mr. Barrow.

Mr. BARROW. I thank the chairman, and with my thanks to the witnesses for their participation, their work and their testimony, I will waive an opening.

OPENING STATEMENT OF HON. BRUCE L. BRALEY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF IOWA

Mr. PALLONE. The gentleman from Iowa, Mr. Braley.

Mr. BRALEY. Thank you, Mr. Chairman. It has been a long time since the word "smite" has been uttered in this hearing room. And unlike my youthful colleague from Connecticut, my three children are in another high risk category, college students. But I am very concerned about the delay in productions of vaccine and the shortages of both the H1N1 and the seasonable flu vaccine and the process of vaccine distribution. There have been severe shortages in my State of Iowa which, by the way, is the number one egg production State in the country, and I would like to speak out on behalf of all eggs who have been criticized.

Vaccine shortages that led to the cancelation of flu shot clinics in my State left thousands of Iowans without access to the flu vaccine and left them vulnerable to the virus. And as of last Friday the Iowa Department of Public Health had confirmed 19 H1N1-related deaths in Iowa, including one child and 18 adults. And those victims include people from Dubuque and Black Hawk Counties, both of which are in my district, and more than 500 Iowans have been hospitalized with the H1N1 virus.

That is why you can imagine how outraged I was to learn a couple of weeks ago that some of the biggest companies in New York, my apologies, Mr. Weiner, including Goldman Sachs, Citigroup, JPMorganChase, and Time Warner, were receiving large doses of this vaccine for their employees. I don't think that it is appropriate or fair that big Wall Street firms be given priority access to the vaccine while thousands of Iowans are going without it.

I sent a letter on November 5th to Secretary Sebelius expressing my serious concerns about the distribution process and urging her to ensure that the vaccine is distributed based on risk and need, not based on wealth or profession or zip code. I haven't received a response to my letter. So I hope that you folks today can shed some light on this process, what additional corrective measures, if any, have been taken and explain to me and my constituents why these companies were receiving the vaccine when so many of my constituents were forced to go without. And I am talking about seniors, immunocompromised individuals and children.

I look forward to hearing the testimony of the witnesses today and learning when the Iowans that I represent who would like to receive these vaccines and would like to receive them soon will receive access and what is being done to promote expansion of the availability of the virus.

So thank you.

[The prepared statement of Mr. Braley follows:]

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Statement of Congressman Bruce Braley
Subcommittee on Health and Subcommittee on Oversight
"H1N1 Preparedness: An Update of Vaccine Production and Distribution"
November 18, 2009

I'd like to begin by thanking Chairman Pallone and Chairman Stupak and the Ranking Members of the Health and Oversight Subcommittees for holding this important hearing today on the production and distribution of the H1N1 flu vaccine. I'm extremely concerned by delays in production of the vaccine, about shortages of the H1N1 and season flu vaccines, and about the process of vaccine distribution.

There have been severe shortages of flu vaccine in my state of Iowa this fall. Vaccine shortages led to the cancelation of flu shot clinics across the state, leaving thousands of Iowans without access to flu vaccines, and leaving them vulnerable to the virus.

As of last Friday, the Iowa Department of Public Health had confirmed 19 H1N1-related deaths in Iowa, including one child and 18 adults. The victims include people from Dubuque and Black Hawk

counties, which are in my district. More than 500 Iowans have been hospitalized with H1N1.

That's why I was outraged to learn a couple of weeks ago that some of the biggest New York companies, including Goldman Sachs, Citigroup, JP Morgan Chase, and Time Warner received doses of the H1N1 vaccine for their employees. I don't believe that it's appropriate or fair for big Wall Street firms to be given priority access to the vaccine while thousands of Iowans were going without.

I sent a letter on November 5 to Secretary Sebelius expressing my serious concerns about this vaccine distribution process and urging her to ensure that the H1N1 vaccine is distributed based on risk and need, not on wealth, profession, or zip code. I have not yet received a response to my letter, so I hope the witnesses here today can shed some light on this process and explain to me and my constituents why New York companies received the vaccine while many of them were forced to go without.

I look forward to hearing the testimony of the witnesses today and to learning when all Iowans who would like to receive the H1N1 or seasonal flu vaccine will have reliable access to this protection.

Mr. PALLONE. The gentleman from Maryland, Mr. Sarbanes.

OPENING STATEMENT OF HON. JOHN P. SARBANES, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MARYLAND

Mr. SARBANES. Thank you, Mr. Chairman. I will be very brief. We are looking forward to your testimony. I will be curious to hear you describe where things have gone compared to where you thought they would be the last time we had a hearing, so that at the beginning of this process you made projections, you talked about certain contingencies, and I would be interested to know how the advance of the disease has panned out against those original projections because it helps us make judgments as you project further. And that would be both with respect to advance of the disease and with respect to the way we are responding to it.

And I just want to echo what Congressman Braley just said, and that is if there are going to be delays in the distribution and if what has been manufactured is less than what we hoped to have at our disposal at this point in time it becomes even more critical—I mean it is always critical that the distribution be done in a fair way, but it becomes even more critical that it be done fairly because the larger context is that there are shortages and it makes people, I think, much more resentful, and rightly so, when they see an unequal distribution and one that is not occurring according to the criteria that you have laid out.

So I think there is probably a lot of interest in having you address that in your testimony. And I yield back my time.

Mr. PALLONE. Thank you, Mr. Sarbanes.

Mr. Engel.

OPENING STATEMENT OF HON. ELIOT L. ENGEL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW YORK

Mr. ENGEL. Thank you very much, Mr. Chairman. And I too will be brief. I am delighted that we are holding this hearing this morning, and I look forward to listening to the witnesses. Obviously what has gone on with the swine flu is something that Americans are asking lots and lots of questions. And we are hearing that this is something that is easily spread and yet we were told several months ago that there would be adequate vaccines and there aren't. And I know people have been contacting my office to find out where they can get vaccines. And I think what happened here is that people's expectations were rising when the government announced that there would be no problem and people would have enough vaccines for use. I think if that had not been stated or said perhaps people's expectations wouldn't be so high. But the double whammy of not having enough vaccines, plus the announcement that there would be enough for people has made people, have made people think that something is terribly wrong.

I have had some discussions with some of the people testifying today, and they have helped me to understand what has happened, but I think that we really need to ensure that something like this really never happens again. I know that people in my district have been wondering. My Staff Director had his two little boys just last

week both come down with swine flu. And people have been calling my office and wanting to know where they can get vaccinated, and we have been trying to help them the best we can. But people are confused and angry at the same time.

So I look forward to the testimony and to hear what the witnesses have to say. And I thank you, Mr. Chairman, for holding this very important hearing, and I yield back.

Mr. PALLONE. Thank you, Mr. Engel. I believe we have concluded our opening statements. So we will now proceed to the witnesses. Let me call or introduce the first panel. Starting with my left is Dr. Anne Schuchat, I hope I am pronouncing it right, who is Director of the National Center for Immunization and Respiratory Diseases at the Centers for Disease Control and Prevention. And then we have Dr. Nicole Lurie, who is the Assistant Secretary for Preparedness and Response at the Department of Health and Human Services. And finally, Dr. Jesse Goodman who is Chief Scientist and Deputy Commissioner for Science and Public Health for the Food and Drug Administration.

Now, in accordance with the policy of the Oversight and Investigations Subcommittee, I have not done this before but because of the policy of the Oversight and Investigations Subcommittee all testimony at today's hearing will be taken under oath. And I am to advise you that you have a right under the rules of the House to be advised by counsel during your testimony. And I have to ask you initially if you wish to be represented by counsel and, if so, you would have to State your counsel's name.

Dr. Schuchat.

Dr. SCHUCHAT. No, thank you.

Mr. PALLONE. No. Dr. Lurie.

Dr. LURIE. No, thank you.

Mr. PALLONE. You said no. And Dr. Goodman.

Dr. GOODMAN. Thank you, no.

Mr. PALLONE. No. OK. So then we are going to stand. Each of you should stand. We are going to take an oath. Or you are going to take an oath I should say.

Let the record reflect that the witnesses replied in the affirmative. You are now under oath. Thank you.

[Witnesses sworn.]

Mr. PALLONE. And we will start with a 5-minute opening statement from Dr. Schuchat. I think you all know that you can submit a longer statement for inclusion in the record, but we would like you try to stick to the 5. Thank you.

TESTIMONIES OF DR. ANNE SCHUCHAT, DIRECTOR, NATIONAL CENTER FOR IMMUNIZATION AND RESPIRATORY DISEASES, CENTERS FOR DISEASE CONTROL AND PREVENTION; DR. NICOLE LURIE, ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE, DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND DR. JESSE GOODMAN, ACTING CHIEF SCIENTIST, DEPUTY COMMISSIONER FOR SCIENTIFIC AND MEDICAL PROGRAMS, FOOD AND DRUG ADMINISTRATION

TESTIMONY OF DR. ANNE SCHUCHAT

Dr. SCHUCHAT. Thank you, Chairmen Pallone and Stupak, Ranking Member Walden, and members of the subcommittee. I am really pleased to be back to talk with the committee about our comprehensive response to the H1N1 pandemic and to answer your questions.

A brief update on the situation. As you've heard, we released new estimates for the toll the virus has taken in the first 6 months of the pandemic: 22 million infected or ill, 98,000 hospitalized and, sadly, almost 4,000 deaths. The virus is spreading in—considered widespread in 46 States. In many areas it is beginning to decrease, the burden of illness, but in some it is still on the upswing. There has been no change in the illness pattern, still disproportionately a younger person's disease, many people with underlying conditions or pregnancy disproportionately affected with severe complications.

So far no change in the virus. It hasn't become more virulent or changed genetically. We still think the vaccine is an excellent match with this virus that is circulating.

But unfortunately, the trajectory that the virus will have is unpredictable. We do not know how long this wave will last, whether there will be multiple waves. We know that flu season can last until May usually. We don't know how much seasonable flu strains we will have, many unknowns. And that makes it even more important that we strengthen our response.

Without the investments of Congress in preparedness and strengthening our ability to cope with a pandemic we would be in much worse shape than we are today. I will go through CDC's response, and others will talk more broadly.

We rapidly identified and characterized the virus, we developed candidate vaccine strains, we carried out epidemiologic and laboratory surveillance in the U.S. and abroad to understand what was going on and direct our interventions. Our aggressive response has been science based. We have rapidly deployed lifesaving anti-viral medicines and other material from our strategic national stockpile. Laboratory kits were prepared in record time and disseminated to all of the public health labs here in the U.S. and to 150 other countries. We deployed field teams to support the State and local response and continue to support the State and locals in what's very much an implementation effort at the front lines.

We have issued science-based guidelines on prevention and mitigation. We expected disease to increase this fall before vaccine was available, so we worked very actively with other sectors to make the best use of antiviral medicines in high risk people or in severe illness, to work with education on ways to better intervene in schools without as disruptive effects as we saw last spring. We fo-

cused on businesses and health care workers, and so forth. Communication has been a priority for all of us and we have done outreach with new media and old media and many partners.

Of course the heart of our response is the vaccination effort right now. It's been unprecedented in the speed with which we've gotten this vaccine. But of course like everyone I am disappointed in the initial production and we've been held captive really to this slow growing virus.

However, today I can announce that there are 49.9 million doses of H1N1 vaccine that are available for the States to order. It's not as much as we wanted to have by now or frankly what we needed to have by now, but every dose that's coming out is being rapidly moved to places where it can go into people and help protect them.

At CDC we work to develop recommendations to prioritize the use of scarce vaccine for those at highest risk of disease or most likely to spread. We have a distribution system that gives each State a pro rata population based share of the vaccine trying to have as fair a process as possible. The States and local health authorities are the implementers. They are deciding where that vaccine gets shipped. They are working very closely with the provider community, the local health departments, hospitals, with community health centers, with others, schools for instance, where vaccination efforts can go forward rapidly.

Thirty-four States so far have initiated school located vaccination efforts to really reach large numbers of children promptly. Not as many have been able to be completed because of the supply but more are happening every day, and we know that the State of Maine expects to finish their school located program by the end of this week.

We've done all this mindful that the environment we live in makes communication and emphasis on the safety of vaccines the forefront for many. And so we've done this without cutting any corners on safety and have strengthened our safety monitoring system to address any unanticipated problems.

We are working hard with partners across government and in particular with the State, local, and tribal authorities who are directing the program where they are. They have been working tirelessly to make this succeed, and I'm happy to detail some of the efforts they've been making in the comment period.

When we have the opportunity to look back on this public health challenge, we'll have time to reflect on the remarkable scientific accomplishments that made it possible to rapidly detect and track a previously unseen virus and get a vaccine developed in record time. We'll have time to more systematically search for lessons in production and delivery that we can apply in a future pandemic and to rebuild the public health system that we all rely on. But today we need to quickly adapt from our recent experience and maintain our focus on the days, weeks and months just ahead.

We'll have more vaccine to put in the path of this virus. And it's our commitment to continue to work closely with our State and local public health partners to ensure that it's as effectively delivered to those who need it most.

I will look forward to answering your questions.

[The prepared statement of Dr. Schuchat follows:]

Testimony before the
Subcommittees on Health, and Oversight and Investigations
Committee on Energy and Commerce
U.S. House of Representatives

H1N1 Preparedness: An Overview of Vaccine Production and Distribution

Rear Admiral Anne Schuchat, M.D.
Assistant Surgeon General
Director, National Center for Immunization and Respiratory Diseases (NCIRD)
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services

For Release upon Delivery
Expected at 10:00 a.m.
November 18, 2009

Chairmen Pallone and Stupak, Ranking Members Deal and Walden, members of the subcommittees, thank you for this opportunity to update you on the public health challenges of 2009 H1N1 influenza.

The Centers for Disease Control and Prevention (CDC) and our colleagues throughout the Department of Health and Human Services (HHS) are working in close partnership with many parts of the federal government, as well as with states and localities, under a national preparedness and response framework for action that builds on the efforts and lessons learned from the past few months, this previous spring and influenza preparedness trainings conducted during the last several years. Working together with governors, mayors, tribal leaders, state and local health departments, the medical community and our private sector partners, we have been monitoring the spread of H1N1 and facilitating prevention and treatment, including implementing a vaccination program. CDC also has deployed staff, both domestically and globally, to assist in epidemiologic investigation of the virus and support state, local and territorial health departments with the H1N1 mass vaccination campaign.

Influenza is probably the least predictable of all infectious diseases, and the 2009 H1N1 pandemic has presented considerable challenges—in particular the delay in production and delivery of a vaccine, in part because of the slow growth of the virus during the manufacturing process. Today I will update you on the overall situation, provide an update on vaccination status, and discuss other steps we are taking to address these challenges.

Tracking and Monitoring Influenza Activity

One major area of effort is the tracking and monitoring of influenza activity, which helps individuals and institutions monitor and understand the impact of the 2009 H1N1 virus. Since the initial spring emergence of 2009 H1N1 influenza, the virus has spread throughout the world. H1N1 was the dominant strain of influenza in the southern hemisphere during its winter flu season. Data about the virus from around the world—much of it collected with CDC assistance—have shown that the circulating pandemic H1N1 virus has not mutated significantly since the spring, and the virus remains very closely matched to the 2009 H1N1 vaccine. This virus also remains susceptible to the antiviral drugs oseltamivir and zanamivir, with very rare exception.

Unlike a usual influenza season, flu activity in the United States continued throughout the summer, at summer camps and elsewhere. More recently, we have seen widespread influenza activity in 48 states; any reports of widespread influenza this early in the season are very unusual. Visits to doctors for influenza-like illness as well as flu-related hospitalizations and deaths among children and young adults also are higher than expected for this time of year, and higher than have been observed at any time in many recent flu seasons. We are also already observing that more communities are affected than those that experienced H1N1 outbreaks this past spring and summer.

Almost all of the influenza viruses identified so far this season have been 2009 H1N1 influenza A viruses. However, seasonal influenza viruses also may cause illness in the upcoming months—getting one type of influenza does not prevent you from getting another type later in the season.

Because of the current H1N1 pandemic, several additional systems have been put in place and existing systems modified to more closely monitor aspects of 2009 H1N1 influenza. These include the following:

Enhancing Hospitalization Surveillance: CDC has greatly increased the capacity to collect detailed information on patients hospitalized with influenza. Using the 198 hospitals in the Emerging Infections Program (EIP) network and 6 additional sites with 76 hospitals, CDC monitors a population of 25.6 million to estimate hospitalization rates by age group and monitor the clinical course among persons with severe disease requiring hospitalization.

Expanding Testing Capability: Within 2.5 weeks of first detecting the 2009 H1N1 virus, CDC had fully characterized the new virus, disseminated information to researchers and public health officials, and developed and begun shipping to states a new test to detect cases of 2009 H1N1 infection. CDC continues to support all states and territories with test reagents, equipment, and funding to maintain laboratory staff and ship specimens for testing. In addition, CDC serves as the primary support for public health laboratories conducting H1N1 tests around the globe and has provided test reagents to 406 laboratories in 154 countries. It is vital that accurate testing continue in the United States and abroad to monitor any mutations in the virus that may indicate increases in infection severity, resistance to antiviral drugs, or a decrease in the match between the vaccine strain and the circulating strain.

Health Care System Readiness: HHS is also using multiple systems to track the impact the 2009 H1N1 influenza outbreak has on our health care system. HHS is in constant communication with

state health officials and hospital administrators to monitor stress on the health care system and to prepare for the possibility that federal medical assets will be necessary to supplement state and local surge capabilities. To date, state and local officials and health care facilities have been able to accommodate the increased patient loads due to 2009 H1N1, but HHS is monitoring this closely and is prepared to respond quickly if the situation warrants.

Implementing a Flu-related School Dismissal Monitoring System: CDC and the U.S. Department of Education (ED), in collaboration with state and local health and education agencies and national non-governmental organizations, have implemented a flu-related school dismissal monitoring system for the 2009-2010 school year. This monitoring system generates a verified, near-real-time, national summary report daily on the number of school dismissals by state across the 130,000 public and private schools in the United States, and the number of students and teachers impacted. The system was activated August 3, 2009. This has helped us to calibrate our messages and guidance and may have contributed to the smaller number of school closings seen in the fall relative to those seen in the spring.

Providing Science-Based Guidance

A second major area of effort in support of individuals and institutions is to provide science-based guidance that allows them to take appropriate and effective action. Slowing the spread and reducing the impact of 2009 H1N1 and seasonal flu is a shared responsibility. We can all take action to reduce the impact flu will have on our communities, schools, businesses, other community organizations, and homes this fall, winter, and spring.

There are many ways to prevent respiratory infections and CDC provides specific recommendations targeted to a wide variety of groups, including the general public, people with certain underlying health conditions, infants, children, parents, pregnant women, and seniors. CDC also has provided guidance to workers and in relation to work settings, such as health care workers, first responders, and those in the swine industry, as well as to laboratories, homeless shelters, correctional and detention centers, hemodialysis centers, schools, child care settings, colleges and universities, small businesses, and federal agencies.

With the holidays coming up, reducing the spread of 2009 H1N1 influenza among travelers will be an important consideration.

CDC quarantine station staff respond to reports of illness, including influenza-like illness when reported, in international travelers arriving at U.S. ports of entry. Interim guidance documents for response to travelers with influenza-like illness, for airline crew, cruise ship personnel and Department of Homeland Security port and field staff have been developed and posted online. As new information about this 2009 H1N1 influenza virus becomes available, CDC will evaluate its guidance and, as appropriate, update it using the best available science and ensure that these changes are communicated to the public, partners, and other stakeholders.

In preparation for the upcoming months when we expect many families and individuals to gather for the holidays, we are preparing to launch a national communications campaign to encourage domestic and international travelers to take steps to prevent the spread of flu. Plans are to display public advertisements with flu prevention messages in ports of entry and various other

advertising locations, such as newspapers and online advertisements, both before and during the upcoming holiday travel season.

Supporting Shared Responsibility and Action through Enhanced Communication

A third major area of effort is to support shared responsibility and action through enhanced communication to individuals. Our recommendations and action plans are based on the best available scientific information. CDC is working to ensure that Americans are informed about this pandemic and consistently updated with information in clear language. The 2009 H1N1 pandemic is a dynamic situation, and it is essential that the American people are fully engaged and able to be part of the mitigation strategy and overall response. CDC will continue to conduct regular media briefings, available at flu.gov, to get critical information about influenza to the American people.

Some ways to combat the spread of respiratory infections include staying home when you are sick and keeping sick children at home. Covering your cough and sneeze and washing your hands frequently will also help reduce the spread of infection. Taking personal responsibility for one's health will help reduce the spread of 2009 H1N1 influenza and other respiratory illnesses.

CDC is communicating with the public about ways to reduce the spread of flu in more interactive formats such as blog posts on the Focus on Flu WebMD blog, radio public service announcements, and podcasts.

Through the CDC INFO Line, we serve the public, clinicians, state and local health departments and other federal partners 24 hours/day, 7 days/week, in English and Spanish both for phone and email inquiries. Our information is updated around the clock so we are well positioned to respond to the needs and concerns of our inquirers. Our customer service representatives get first-hand feedback from the public on a daily basis. In addition to the H1N1 response, we continue to provide this service for all other CDC programs.

Prevention through Vaccination

A fourth major area of effort is prevention through vaccination. Vaccination is our most effective tool to reduce the impact of influenza. Working in close partnership with industry, HHS has led the process of developing a safe and effective 2009 H1N1 influenza vaccine, but the delivery of vaccine to the public has not been as rapid as hoped or initially estimated. CDC, in collaboration with the Food and Drug Administration (FDA), characterized the virus, identified a candidate vaccine strain, and our HHS partners expedited manufacturing, initiated clinical trials, and licensed four 2009 H1N1 influenza vaccines all within five months. The speed of this vaccine development was made possible due to investments made in vaccine advanced research and development and vaccine manufacturing infrastructure building through the office of the Assistant Secretary for Preparedness and Response (ASPR), Biomedical Advanced Research and Development Authority (BARDA) over the past four years, and in collaboration with CDC, the National Institutes of Health (NIH), and FDA. The rapid responses of HHS agencies, in terms of surveillance, viral characterization, pre-clinical and clinical testing, and assay development, were greatly aided by pandemic preparedness efforts for influenza pandemics set in motion by the H5N1 virus re-emergence in 2003, and the resources Congress provided for those efforts.

Pandemic planning had anticipated vaccine becoming available 6-9 months after emergence of a new influenza. In fact, 2009 H1N1 vaccination began in early October—just 5 months after the emergence of 2009 H1N1 influenza. Critical support from Congress resulted in $1.44 billion for states and hospitals to support planning, preparation, and implementation efforts. States and cities began placing orders for the 2009 H1N1 vaccine on September 30th. The first vaccination with 2009 H1N1 influenza vaccine outside of clinical trials was given October 5th. Tens of millions of doses have become available for ordering, and millions more become available each week. Although the initial pace of vaccine delivery to the States has complicated the early immunization efforts, vaccine will become increasingly available over the weeks ahead, and will become more visible through delivery in a variety of settings, such as vaccination clinics organized by local health departments, healthcare provider offices, schools, pharmacies, and workplaces.

States have begun executing their plans to provide vaccine to targeted priority populations, and CDC continues to offer technical assistance to states and other public health partners as we work together to ensure the H1N1 vaccination program is as effective as possible. Although we had hoped to have more vaccine distributed by this point, we are working hard to get vaccine out to the public just as soon as we receive it.

H1N1 vaccines are manufactured by the same companies employing the same methods used for the yearly production of seasonal flu vaccines. H1N1 vaccine is distributed to providers and state health departments similarly to the way federally purchased vaccines are distributed in the

Vaccines for Children program. Two types of 2009 H1N1 vaccine are now available: injectable vaccine made from inactivated virus, including thimerosal-free formulations, and nasal vaccine made from live, attenuated (weakened) virus.

CDC's Advisory Committee on Immunization Practices (ACIP) has recommended that 2009 H1N1 vaccines be directed to target populations at greatest risk of illness and severe disease caused by this virus. On July 29, 2009, ACIP recommended targeting the first available doses of H1N1 vaccine to five high-risk groups comprised of approximately 159 million people; CDC accepted these recommendations. These groups are: pregnant women; people who live with or care for children younger than 6 months of age; health care and emergency services personnel; persons between the ages of 6 months through 24 years of age; and people from ages 25 through 64 years who are at higher risk for severe disease because of chronic health disorders like asthma, diabetes, or compromised immune systems. In addition, ACIP recommended that local public health authorities may want to prioritize a smaller group of people while supplies are limited, in which case the following groups who are at the highest risk for infection or severe illness should receive the vaccine before others: pregnant women, people who live with or care for children younger than 6 months of age, health care and emergency medical services personnel with direct patient contact, children 6 months through 4 years of age, and children 5 through 18 years of age who have chronic medical conditions. This subset of the five target groups comprises approximately 42 million persons in the United States. These recommendations provide a framework from which states can tailor vaccination to local needs.

Ensuring a vaccine that is safe as well as effective is a top priority. CDC expects that the 2009 H1N1 influenza vaccine will have a similar safety profile to seasonal influenza vaccine, which historically has an excellent safety track record. So far the reports of adverse events among H1N1 vaccination are generally mild and are similar to those we see with seasonal flu vaccine. We will remain alert, however, for the possibility of rare, severe adverse events that could be linked to vaccination. CDC and FDA have been working to enhance surveillance systems to rapidly detect any unexpected adverse events among vaccinated persons and to adjust the vaccination program to minimize these risks. Two primary systems used to monitor vaccine safety are the Vaccine Adverse Events Reporting System (VAERS), jointly operated between CDC and FDA, and the Vaccine Safety Datalink (VSD) Project, a collaborative project with eight managed care organizations covering more than nine million members. These systems are designed to determine whether adverse events are occurring among vaccinated persons at a greater rate than among unvaccinated persons. CDC has worked with FDA and other partners to strengthen these vaccine safety tracking systems and we continue to develop new ways to monitor vaccine safety, as announced earlier this week by the Federal Immunization Safety Task Force in HHS. In addition, based on the recommendation of the National Vaccine Advisory Committee (NVAC), HHS established the H1N1 Vaccine Safety Risk Assessment Working Group to review 2009 H1N1 vaccine safety data as it accumulates. This working group of outside experts will conduct regular, rapid reviews of available data from the federal safety monitoring systems and present them to NVAC and federal leadership for appropriate policy action and follow-up.

More than 36,000 people die each year from complications associated with seasonal flu. CDC continues to recommend vaccination against seasonal influenza viruses, especially for all people 50 years of age and over and all adults with certain chronic medical conditions, as well as infants and children. As of the fourth week in October, 89 million doses of seasonal vaccine had been distributed. It appears that interest in seasonal flu vaccine has been unprecedented this year. Manufacturers estimate that a total of 114 million doses will be brought to the U.S. market.

Reducing the Burden of Illness and Death through Antiviral Distribution and Use

In the spring, anticipating commercial market constraints, HHS deployed 11 million courses of antiviral drugs from the Strategic National Stockpile (SNS) to ensure the nation was positioned to quickly employ these drugs to combat 2009 H1N1 and its spread. In early October, HHS shipped an additional 300,000 bottles of the oral suspension formulation of the antiviral oseltamivir to states in order to mitigate a predicted near-term national shortage indicated by commercial supply data. In addition, the Secretary authorized the release of the remaining 234,000 bottles of pediatric Tamiflu® on October 29th. We will continue to conduct outreach to pharmacists and providers related to pediatric dosing and compounding practices to help assure supplies are able to meet pediatric demand for antiviral treatment, and we have updated our guidance relating to general antiviral use as new information has warranted. Finally, CDC and FDA have also worked together to address potential options for treatment of seriously ill hospitalized patients with influenza, including situations in which physicians may wish to use investigational formulations of antiviral drugs for intravenous therapy. The FDA issued an emergency use authorization (EUA) on October 23rd, 2009, for the investigational antiviral drug peramivir intravenous (IV) authorizing the emergency use of peramivir for the treatment of

certain hospitalized adult and pediatric patients with confirmed or suspected 2009 H1N1 influenza infection. Physician requests for peramivir to be used under the EUA are managed through a CDC web portal.

Closing Remarks

CDC is working hard to limit the impact of this pandemic, and we are committed to keeping the public and the Congress fully informed about both the situation and our response. We are collaborating with our federal partners as well as with other organizations that have unique expertise to help CDC provide guidance to multiple sectors of our economy and society. There have been enormous efforts in the United States and abroad to prepare for this kind of challenge.

Our nation's current preparedness is a direct result of the investments and support of Congress over recent years, effective planning and action by Federal agencies, and the hard work of state and local officials across the country. We look forward to working closely with Congress as we address the situation as it continues to evolve in the weeks and months ahead.

Again, Mr. Chairman, thank you for the opportunity to participate in this conversation with you and your colleagues. I look forward to answering your questions.

Mr. PALLONE. Thank you, Dr. Schuchat.
Dr. Lurie.

TESTIMONY OF DR. NICOLE LURIE

Dr. LURIE. Thank you. I, too, am very pleased to be able to talk to you today about our pandemic response.

Mr. PALLONE. Maybe put that mic a little closer to you there.

Dr. LURIE. Is that better?

Mr. PALLONE. Yes. Talk into it directly if you can.

Dr. LURIE. Thank you for your foresight in helping to rebuild our country's vaccine infrastructure. As a result, when we decided to pursue vaccine for H1N1 this spring we had preexisting contracts with manufacturers already licensed in the U.S. to get us out of the block quickly to contract for manufacturing vaccine and preparedness efforts have helped hospitals and health care systems also be ready.

My office has a four-fold response related to this pandemic: First, to coordinate across department response and work with the interagency; secondly, to stimulate the development of and contract with for vaccines and antivirals; third, to monitor and ensure that we can backstop States and communities if they get overwhelmed and request our help; and finally, to stay prepared for any other emergency, not to take our eye off the ball.

This whole response has been a public-private partnership from the get-go. Starting with vaccines, as you know, we developed a new vaccine with unprecedented speed. And this was really made possible by investments in basic and clinical science, manufacturing regulatory processes, and would not have been possible at all without our partnerships with industry. And while modest amounts of vaccine came ahead of schedule, as the graphic over here details on the left, a combination of poor production yields, late completion of seasonable vaccine, problems with new filling lines, decisions in the home country of one manufacturer, cost delays in the availability of vaccine, not just for the U.S. but around the world. And while the number of doses that's been produced and distributed and administered continue to grow we remain vigilant.

To ensure a steady supply of vaccines we talk with manufacturers almost every single day. We constantly monitor the progress of every lot produced, working to make up ground wherever possible. And right now we have full time staff in the facilities of two of the manufacturers.

In addition, Secretary Sebelius and I have spoken directly with CEOs actually on several occasions seeking to identify opportunities to work together to be sure that there are no arcane kinds of obstacles in the way. And while these delays are really frustrating to everyone, we do need to remember that the virus is the real enemy here. And the way forward, as we've been talking about this morning, is to improve our country's domestic manufacturing capacity, using newer, faster and more predictable technology so that the virus of the future does not defeat us.

Antivirals have been another critical aspect of our response, and I just want to point out that we supported the development of new antivirals, issuing the first emergency use authorization for an in-

travenous antiviral, and we have procured over 30,000 doses across three types of antiviral drugs.

We are also focused on ensuring the health care system and communities throughout the country remains able to care for those who need it. CMS can now grant 1135 waivers to decompress hospitals and other facilities when they are getting overburdened, letting them use those emergency plans. And we stand ready to deploy Federal assets when necessary, including vaccination teams, clinical and laboratory staff, and temporary medical facilities. And our first ever vaccination team is headed to Delaware to do just that.

We have also partnered closely with the private sector health care system, including health insurers, pharmacists, big box stores, AMA, and the public health community to find ways to pay for vaccine administration so cost is not a barrier to people who want to be vaccinated.

Let me shift for a minute to lessons learned. Clearly the support of Congress in the past few years have been critical in enabling us to respond so quickly to this pandemic. And yet it is clear the chronic underinvestment in public health, whether at the Federal, State or local levels or on the manufacturing infrastructure, has real world consequences, and we cannot afford to let this happen again ever.

While we have made vaccine in record time without cutting any corners, in retrospect our original projections were based on the collective experience with seasonable flu and with H5N1 vaccine manufacturing, and we are optimistic in the face of what's proved to be a daunting challenge provided by Mother Nature, and despite the best efforts of Federal Government and our partners in the private sector.

Congress and the public have rightfully asked for projections about numbers of doses, and we want to be transparent, but at the same time provide all of the caveats about the uncertain nature of these projections.

This has been a real challenge, especially as measures are captured with shorter and shorter sound bites that omit detail about such caveats, and this has led to frustration for everyone involved, especially the public.

As an important part of this transparency and part of our public-private partnership we will start releasing this week, together with all five vaccine manufacturers, the number of projected doses by manufacturer for successive 2-week periods.

In this past week storm-related delays nearly derailed shipment of vaccine to many States from Maine to Alabama. And I want to credit the hard work of CDC and ASPR staff who worked all weekend to be sure the vaccine could be ordered and shipped so the clinics could go on as planned.

But we are far from done with the science of advanced development related to vaccines and with building manufacturing capacity in the United States. We are excited that the first cell based facility will open or have its ribbon cutting next week in North Carolina.

But my fear frankly is when this is over we will decide we don't need to worry about a pandemic for the next 30 years. Nothing could be more dangerous. Despite these challenges, I think that

much of what we have learned and frankly continue to learn through this pandemic and in the investments we have made to address it will serve us well in confronting future public health emergencies as well as for day-to-day public health for years to come.

I, too, look forward to your questions.

[The prepared statement of Dr. Lurie follows:]

Testimony
Committee on Energy and Commerce
Subcommittee on Oversight and Investigations and
Subcommittee on Health
United States House of Representatives

Safeguarding our Nation: HHS Response to the H1N1 Outbreak

Statement of
Nicole Lurie, MD, MSPH
Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services

For Release on Delivery
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Tuesday, November 18, 2009

Good morning Chairmen Pallone and Stupak, Ranking Members Deal and Walden, and Members of the two Subcommittees. I am Dr. Nicole Lurie, the Assistant Secretary for Preparedness and Response (ASPR) at the U.S. Department of Health and Human Services (HHS). As Secretary Sebelius emphasized in her testimony before the Senate in October, slowing the spread and reducing the impact of 2009 H1N1 is a shared responsibility, and we all need to plan for what would need to be done as the flu impacts our communities, schools, businesses, and homes this fall. I appreciate the opportunity today to discuss our role as well as some of the challenges and successes we have encountered in responding to the 2009 H1N1 influenza outbreak.

Before I go further, let me take the opportunity to thank you not only for the rapid congressional appropriations to respond to this current influenza threat but also for the foresight in providing significant resources since FY 2006 to lay the foundation for our Nation's pandemic preparedness. These resources have demonstrated a strong return on investment and have dramatically improved our ability to respond. However, our work in this area is far from done. We look forward to working with you and your congressional colleagues in the future to continue to build our response capabilities not only for an influenza virus but also the wide range of natural and manmade threats that we face.

Overview of the Outbreak

Since the initial spring outbreak of 2009 H1N1 influenza, this virus has triggered a worldwide pandemic, and was the dominant flu strain in the southern hemisphere during that hemisphere's winter flu season. Data about the virus from around the world have shown that the circulating pandemic H1N1 virus has not mutated significantly since the spring. The virus remains similar to the virus chosen for the 2009 H1N1 vaccine, and remains susceptible to the antiviral drugs oseltamivir (Tamiflu) and zanamivir (Relenza), with rare exception. As with seasonal influenza, persons with some chronic health disorders and pregnant women have a higher risk of severe disease. In contrast to seasonal influenza, elderly persons have proven less likely to contract the virus; nevertheless, many elderly persons who do contract the virus have had serious complications. Early treatment with antivirals is recommended for elderly persons as well as for pregnant women, others at high risk for complications, and for anyone who becomes seriously ill.

Unlike our typical seasonal flu, we continued to see flu activity in the United States over the summer, notably among school-aged children and young adults. More recently, we have seen widespread influenza activity in almost all states. Visits to doctors for influenza-like illness are much higher than levels expected for this time of the year.

Over the next several months, seasonal influenza viruses may circulate along with the 2009 H1N1 influenza virus, and it will not be possible to determine quickly if ill individuals have 2009 H1N1 influenza, seasonal influenza, or other respiratory conditions based on symptoms alone. Because of this, close monitoring of viruses in the United States will be critical to ensure that the best guidance about treatment and prevention of influenza can be provided.

Office of the Assistant Secretary for Preparedness and Response (ASPR)

The Pandemic and All-Hazards Preparedness Act (the Act) designated the HHS Secretary as the lead Federal official for public health and medical response to public health emergencies and incidents covered by the National Response Plan developed pursuant to section 502(6) of the Homeland Security Act of 2002, or any successor plan, and created the Assistant Secretary for Preparedness and Response. Under the Act, ASPR plays a pivotal role in coordinating emergency response efforts across the various HHS agencies and among our federal interagency partners.

2009 H1N1 Task Force

In July 2009, the White House National Security Staff (NSS) released the *National Framework for 2009 H1N1 Influenza Preparedness and Response (National Framework)* to ensure a coordinated and focused national strategy. In response, ASPR created the 2009 H1N1 Task Force to: coordinate and consolidate H1N1 strategic program activities; serve as the focal point for policy

coordination; and ensure that HHS's National Framework activities and accomplishments are reported to DHS according to NSS timelines.

The Task Force addresses the National Framework's four key capability "pillars:" surveillance, mitigation measures, vaccination, and communication and education. The Task Force meets regularly with me and the HHS Chief of Staff to review ongoing activities to ensure our successful execution of the National Framework strategy. The Task Force has closely collaborated with DHS to establish a Common Operating Picture (COP) for 2009 H1N1, a single display of relevant information to facilitate collaborative planning and to achieve situational awareness.

ESF #8 Response Activities

Under the National Response Framework, ASPR is responsible for coordinating the Emergency Support Function (ESF) #8 response – Public Health and Medical Services. ASPR provides the mechanism for coordinated federal assistance to supplement State, local, territorial and tribal resources in response to public health and medical care needs during an emergency.

Specifically with regard to the 2009 H1N1 influenza outbreak, ASPR coordinates the interagency public health and medical response activities through a series of twice-weekly ESF #8 calls. During these calls, HHS regional health administrators and regional emergency coordinators report updates on their

regions' pandemic influenza preparedness and response activities. Federal interagency partners also report their activities for group discussion and integration.

Other coordination activities include weekly calls between ASPR and the State health departments to discuss any challenges and issues that might necessitate federal assistance. ASPR has also conducted calls with intensive care physicians to better understand the clinical picture of patients requiring extensive care in hospitals and to share information and experience to help identify best practices to improve patient outcomes. One of our critical concerns is to prevent local healthcare system failures from becoming regional healthcare system failures. Proactive measures to support our local partners in preventing system failure include 1135 waivers to decompress overburdened hospitals and deploying federal assets (where necessary) including clinical staff, temporary medical facilities and any needed logistical support.

Hospital Preparedness

Since its inception in 2002, ASPR's Hospital Preparedness Program (HPP) has provided more than $3 billion to fund the development of medical surge capacity and capability at the State and local level. HPP funds are awarded to State and territory departments of public health, which in turn fund projects at hospitals and other healthcare entities. As a result, hospitals can now communicate with other responders through interoperable communication systems; track bed and

resource availability using electronic systems; protect their healthcare workers with proper equipment; train their healthcare workers on how to handle medical crises and surges; develop fatality management, hospital evacuation, and alternate care plans; and coordinate regional training exercises.

As a result of Congress's investment in the Hospital Preparedness Program our hospitals are better prepared to respond to the current 2009 H1N1 outbreak. Since the inception of funding, pandemic influenza preparedness and development of alternative care sites have been two priorities of the HPP program. In 2007, $75 million was awarded to States and territories specifically for pandemic influenza planning, including pandemic exercises and purchases of equipment, such as ventilators, that would aid in their response to a pandemic. Of the grantees receiving these funds, 79% conducted pandemic influenza exercises to hone their preparedness capabilities. In 2009, $90 million was awarded from the Supplemental Appropriations Act, 2009 for purchase of personal protective equipment, such as N-95 respirators for healthcare workers, and to develop plans for alternative care sites. CDC has also been providing support to States for vaccine program implementation and to help State and local health departments.

HPP has required recipients to implement a system of bed counting, called the "Hospital Available Beds in Emergencies and Disasters" (HAvBED). This system requires reports of available beds, including a count of available adult and

pediatric general beds and ICU beds, to State and HHS emergency operations centers within four hours of request. For the past couple of months, HAvBED has been operational and collecting information from States about hospital status and has enhanced our 2009 H1N1 medical surge response.

Furthermore, based on the lessons learned from the spring 2009 H1N1 response, HAvBED was modified to also collect information on emergency department stress and hospital stress. ASPR worked with the HPP grantees, the American Hospital Association and private vendors to develop a core set of measures (including daily census counts and equipment shortages) for the level of stress on the healthcare system. Within 48 hours of receiving information, we have senior ASPR experts discuss and analyze data to determine if any hospitals are showing signs of stress or if there are indicators of equipment shortages. On occasions where the data indicates stress, we engage our Regional Emergency Coordinators to work with State health departments in conducting an investigation. To date, state and local officials have been able to accommodate the increased patient loads, but this is something we monitor very closely, and are prepared to respond quickly if the situation warrants. In addition, the declaration by the President of H1N1 as a national emergency, coupled with the Secretary's Declaration of a Public Health Emergency, allows us to temporarily waive legal provisions or modify certain Medicare, Medicaid, CHIP, and HIPAA requirements under the Secretary's waiver authority under Section 1135 of the Social Security Act. This authority can provide hospitals with additional flexibility

in certain circumstances to deal more effectively with patient surge rather than restrictive paperwork. This move has been welcomed by local hospitals many of whom can now make requests of the Centers for Medicare and & Medicaid Services for 1135 waivers in anticipation of increased patient loads. These requests are reviewed within 24 hours and can be granted retroactively to the beginning of the emergency period (that is, back to October 23, 2009) if needed.

Other Activities

ASPR is working with the Society for Critical Care Medicine and has conducted a ventilator survey that will enable HHS to understand how many ventilators are available and where any regional shortages might exist. We are also working with professional organizations to train physicians in care of patients on ventilators.

The National Disaster Medical System (NDMS) has trained personnel to become vaccinators to assist State and local jurisdictions in that activity. Additionally, NDMS teams have received training on 2009 H1N1 influenza and are standing by, ready to assist States/locals in the delivery of care to pandemic influenza patients or to augment non-flu treatment needs so that hospitals can divert their internal resources to H1N1 if needed.

Responding to H1N1

Responding to 2009 H1N1 influenza has provided challenges and valuable lessons that will assist our response efforts going forward. As this emergency unfolded, it became clear that significant resources would be necessary to respond to the pandemic with potentially large impacts. Further, based on a number of factors such as state readiness and vaccine effectiveness, we would not be able to plan response requirements with certainty and thus, how resources would need to be allocated. As a result, we greatly appreciate the flexible funding that the Congress provided for these efforts.

As we learn from the experiences of 2009 H1N1, we look forward to working with you to improve strategies to ensure that our Nation has the right assets at the right time to minimize the health impacts of an influenza pandemic, hurricane or bioterrorism event. The timely access to a flexible response fund has provided us with a nimbleness to quickly augment capabilities – such as hiring personnel on the front line of public health – where the speed of our response translates to lives saved.

Now, I will briefly discuss both our response efforts and a few of the challenges we encountered in our vaccine research and development, antiviral stockpiling, situational awareness, private sector collaboration, and international assistance.

Vaccine Research and Development

ASPR's investment over the past six years in medical countermeasure advanced research and development enabled the Department to complete 2009 H1N1 vaccine development with unprecedented speed. ASPR's Biomedical Advanced Research and Development Authority (BARDA) has worked with industry to build and sustain a domestic manufacturing infrastructure. Under the *HHS Pandemic Influenza Plan* (November 2005), the Department's key goals for vaccine preparedness were:

- Stockpile enough pre-pandemic influenza vaccines to cover 20 million persons in the critical workforce;
- Develop sufficient domestic manufacturing capacity to produce pandemic vaccine for the entire U.S. population of just over 300 million persons within six months of pandemic onset.

To establish domestic pre-pandemic influenza vaccine stockpiles, BARDA supported the development and manufacture of vaccines against different H5N1 avian virus strains. Today, BARDA continues to support a secure supply of raw materials, including eggs for domestic manufacturing of seasonal and novel influenza vaccines and the development and manufacturing of novel influenza vaccine candidates for clinical evaluation. BARDA also provided cost-sharing support to expand the domestic influenza vaccine manufacturing infrastructure by retrofitting existing vaccine manufacturing facilities and building new cell-based influenza vaccine manufacturing facilities. This facility will be operational in

2010. Additionally, FDA was fully engaged with industry to substantially increase the number of US licensed seasonal influenza vaccine manufacturers and their overall production capacity, a necessary infrastructure for pandemic vaccine development and production. It was through the licensed seasonal influenza vaccine framework that we were able to license and rapidly make available H1N1 vaccine.

The rapid responses of HHS agencies, including CDC, the National Institutes of Health, and the Food and Drug Administration, in terms of surveillance, viral characterization, pre-clinical and clinical testing, and assay development, were greatly aided by preparedness efforts for influenza pandemics set in motion by the H5N1 outbreak in 2003. Stockpiling for pandemic preparedness began in 2004, with H5N1 vaccine (23 million doses). In 2005 and 2006, the first six contracts for cell-based vaccines were initiated with manufacturers at a cost of $1.3 billion. In 2007, two manufacturers were contracted for work on adjuvants, which are vaccine-boosting compounds ($137.5 million). Throughout, clinical studies have been supported by ASPR/BARDA and the National Institutes of Health/ National Institute of Allergy and Infectious Diseases (NIH/NIAID).

These initial activities to prepare for H5N1 provided valuable lessons that have informed our efforts to respond to the current 2009 H1N1 outbreak. We learned, for example, that coordination between ASPR/BARDA, CDC, NIH/NIAID and

FDA was necessary to learn about the immunogenic properties of the virus and to conduct clinical trials. Working with our industry partners, we learned that, just as for seasonal influenza vaccines, one dose of the H1N1 vaccine induces a response that is likely to be protective in adults and older children. We also learned that vaccine distribution through Points of Distribution (POD) should not be the only option considered. Instead, we need to develop our planning and contractual relationships to allow for flexible distribution--in this case, through a third-party--to 150,000 State-specified locations.

Since September 30, when the 2009 H1N1 vaccine was first made available to states to distribute, the number of doses that has been produced, distributed, and administered has grown steadily, and states are executing their plans for providing vaccine to high-priority populations. Our goal is to ensure that everyone who wants to get vaccinated will ultimately be able to do so. While modest amounts of vaccine have been made available ahead of schedule, poor production yields with the initial vaccine strains; late completion of seasonal influenza vaccine manufacturing; and equipment failures on new production lines have caused significant delays in the manufacturers' timelines. In addition, one country where vaccine is manufactured claimed priority for their vaccine, resulting in a reduced amount of anticipated H1N1 vaccine available to the US. These delays are affecting both the U.S. and global H1N1 vaccine supplies.

Manufacturers assure us they are taking active steps to overcome the remaining challenges, and we are doing all in our power to help them.

Moreover, BARDA conducts regular site visits to the vaccine manufacturers and constantly monitors the progress of every lot produced, working to make up ground wherever possible. We also now have full time staff at two of the facilities to monitor and assist in addressing any problems that may occur. FDA has been actively involved in the review and approval of new fill and finish facilities to increase capacity. Finally, on October 29, Secretary Sebelius personally spoke with the CEOs of each of the five manufacturers to emphasize the importance of accelerating production in the coming weeks, and I had additional calls with the CEOs last week.

Our experience with the ups and downs of the vaccine manufacturing process has made clear the need to enhance our country's vaccine manufacturing capability. Going forward, HHS planning efforts will continue to support the advanced development of seasonal and pandemic influenza vaccines. In 2005 and 2006, the first six contracts for advanced development of cell-based influenza vaccines were initiated. Several of these contractors have made significant advances toward U.S. licensure of their cell-based influenza vaccines. In 2008, one of these contractors started to build a new state-of the-art cell-based influenza vaccine manufacturing facility with a surge production capacity of 150 million doses of pandemic vaccine in six months using HHS/ASPR

support. Additionally, HHS is supporting the advanced development of a recombinant influenza vaccine, which promises to have a shorter timeframe for production of pandemic vaccines and expects to fund development of more recombinant vaccines soon. HHS also provided cost-sharing support to expand the domestic influenza vaccine manufacturing infrastructure by retrofitting existing domestic vaccine manufacturing facilities, securing year-round supply of eggs and other supplies for existing U.S.-based egg-based facilities, and supported the construction of new U.S.-based cell-based influenza vaccine manufacturing facilities. These investments will advance U.S. pandemic preparedness goals and decrease dependence on foreign manufacture of influenza vaccines.

Antiviral Stockpiling

Under the *HHS Pandemic Influenza Plan*, HHS was required to:

- Establish national influenza antiviral drug stockpiles to treat 25 percent of the U.S. population during a pandemic, plus an immediate readiness cache of 6 million treatment courses for containment at pandemic onset;
- Support the advanced development of new and promising influenza antiviral drugs toward U.S. approval; and
- Boost U.S.-based production of antiviral drugs.

To accomplish these mandates, ASPR awarded contracts in 2004-2007 totaling more than $924 million to establish and coordinate the federal and State pandemic stockpiles of antiviral drugs. We procured 50 million treatment courses for storage in the Strategic National Stockpile (SNS) by the end of 2007, completing the federal contribution to the antiviral goal. Additionally, using funding provided by Congress, ASPR subsidized States in their purchase of 25 million treatment courses of antivirals towards the 31 million treatment course goal for State stockpiles.

In the spring, anticipating commercial market constraints, HHS deployed 11 million courses of antiviral drugs from the Strategic National Stockpile (SNS) to ensure the nation was positioned to quickly employ these drugs to combat H1N1 and its spread. This action has been effective in allowing the nation to deal with spot shortages of antiviral drugs and limitations on supplies of products targeted for young children, including liquid preparations authorized for emergency use in infants less than 1 year of age. To replenish the SNS, HHS purchased 13 million treatment courses ($260 million) of Tamiflu® (10.4 million treatment courses) and Relenza® (2.6 million treatment courses). In October, HHS made available to states an additional 300,000 regimens of the antiviral pediatric oral suspension to mitigate a predicted near-term national shortage indicated by commercial supply data.

To support antiviral development and manufacturing ramp-up activities, BARDA awarded a contract in 2007 for $102.7 million for advanced development and domestic industrialization of a new influenza antiviral drug. Beginning in 2008, BARDA also solicited and awarded additional contracts for new and combination influenza antiviral drugs. These efforts directly benefited pediatric and critically ill populations.

We know that antiviral resistance is a threat. So our acquisition strategy for additional antivirals needed to be flexible. A lesson learned from the 2009 H1N1 outbreak is that rare cases of H1N1 have been Tamiflu resistant. As a result, ASPR has increased efforts to stockpile an alternative antiviral, Relenza. We also know from this outbreak that children are disproportionately affected by 2009 H1N1 influenza, leading us to procure more pediatric courses of antivirals.

Another challenge presented by 2009 H1N1 influenza is the treatment of critically ill individuals, who potentially may require an intravenous antiviral formulation. Currently there are no influenza antiviral drugs licensed for parenteral use (such as I.V.), and further research is important to determine optimal therapy in this setting. Since January 2007, HHS has supported the advanced development of a new antiviral drug, Peramivir, which may be administered intravenously to hospitalized influenza patients. Intravenous administration may provide more dependable dosing for those critically ill patients who have seriously limited ability to absorb drugs given through the gastrointestinal tract, and it is hoped they

might offer a clinical benefit for that reason. On October 23, an Emergency Use Authorization was issued by the FDA for the utilization of Peramivir to treat critically ill patients with H1N1 virus infections. In addition, intravenous formulations of two other antiviral drugs, oseltamivir and zanamivir, for which other formulations are already approved, are being studied. ASPR is procuring intravenous (I.V.) influenza antiviral drugs for stockpiling to be used under Emergency Use Authorization.

Situational Awareness

Situational awareness is an essential component of any incident response. During the 2009 H1N1 influenza response, HHS worked very closely with the Department of Homeland Security (DHS) to develop a National Situation Report (SitRep) which is then inserted into the Homeland Security Information Network (HSIN). Working cooperatively, DHS and HHS have modified the SitRep to accurately reflect public health and medical issues. HHS has also been working with DHS to enable State and local public health officials to gain access to the HSIN so they can maintain their situational awareness.

Public-Private Sector Collaboration

HHS has engaged many private sector partners in a series of problem-solving dialogues related to the vaccine dispensing program. The Association of State and Territorial Health Officials (ASTHO) worked with ASPR to convene a series of meetings with America's Health Insurance Plans (AHIP), individual insurers,

American Pharmacists Association, retail pharmacy chains, American Medical Association (AMA), National Vaccine Program Office, and other State and federal partners. The private sector demonstrated a firm commitment to working through complex issues of vaccine administration, billing processes, and other policy issues that would facilitate a successful vaccine campaign with the goal of providing easy access to the 2009 H1N1 influenza vaccine for every person in the United States who wants it.

Many issues related to vaccine administration, including billing and payment issues, were raised. Partnerships with the HHS Centers for Medicare & Medicaid Services and the AMA yielded the development of specific vaccine codes, and unique vaccine administration codes for both Medicare recipients and the privately insured. In addition, the health insurers and pharmacies agreed upon a set of principles for billing practices and payment procedures and developed associated draft templates to support State vaccine program consistency.

International Assistance

There is broad international recognition that the 2009 H1N1 pandemic is a global health challenge. Millions of people around the world have been affected, thousands have died and the virus continues to spread across international borders. Like most diseases, 2009 H1N1 infection knows no borders. The health of the American people is inseparable from the health of people around the world. Early in the outbreak, HHS and other federal agencies received

multiple requests for international assistance. HHS has provided 769 laboratory and diagnostic kits to 147 countries, 400,000 treatment courses of antivirals to Mexico and 420,000 treatment courses to the Pan American Health Organization to provide assistance to Latin America and the Caribbean. Similarly, the U.S. Government has received requests for more than 30 million doses of vaccine from 21 countries. Recognizing the needs of developing countries, President Obama committed to make 10 percent of the US 2009 H1N1 vaccine supply available to them through the World Health Organization (WHO). Vaccine will be donated on a rolling basis, as it becomes available, in order to assist countries that will not otherwise have direct access to the vaccine. We are taking this action in concert with international partners: Australia, Brazil, France, Italy, New Zealand, Norway, Switzerland, Japan, Germany, and the United Kingdom.

On October 5, we met with the Governments of Mexico and Canada to review current 2009 H1N1 efforts and decided to re-institute the North American Plan for Avian and Pandemic Influenza Coordinating Body to ensure continued international coordination in the areas of human health, animal health, border issues and emergency management. On October 31, Secretary Sebelius discussed efforts to coordinate donor contributions, maximize the impact of our collective efforts, and mitigate the effects of this pandemic on the poorest regions of the world with the World Health Organization (WHO) Director General, United Nations System Influenza Coordinator (UNSIC), United Nations Secretary General, and United Nations Children's Fund (UNICEF) Executive Director.

Conclusion

I want to assure the Subcommittees that the Administration is taking the public health challenges of 2009 H1N1 seriously and is implementing a comprehensive strategy to monitor and address this influenza outbreak throughout the fall and winter. HHS continues to work in close partnership with virtually every part of the federal government under a national preparedness and response framework for action that builds on the efforts and lessons learned from this spring.

Working together with governors, mayors, tribal leaders, state and local health departments, the medical community, and our private sector partners, the federal government has been actively implementing a vaccination program and continues to revise and refine our pandemic influenza plans and activities based on new data and information.

It is important to reiterate that our current level of preparedness and subsequent ability to respond is a direct result of the investments and support of Congress; the hard work of State, local, tribal, and territorial public health officials; and our partners in the private and not-for-profit sectors. Building strong systems to track and monitor seasonal influenza has allowed us to closely monitor the impact of this novel virus on our communities.

Our Nation's investment in public health infrastructure, particularly at the state and local levels, remains a critical challenge that has real life consequences.

Today, these consequences are impacting our communities, our schools, our workplaces and our homes.

Investments in science and the public health infrastructure will enable us to better prepare and respond to threats, such as 2009 H1N1, that arise in the future. For instance, the President's 2010 budget includes funding for advanced development of antiviral drugs and invests in new vaccine technology. This will advance our on-going commitments to developing new cell-based and recombinant vaccine production methods and help complete a domestic cell-based production facility, currently under construction here in the U.S. In addition, our work on new antivirals and important medical devices, including rapid diagnostics, continues to yield exciting results. These investments hold the promise of more effective treatments that can be developed over shorter timeframes and made available more quickly to families and individuals. It is also critical to increase investments in our State and local health departments, which have been chronically underfunded. We have made great strides in leveraging information technology to enhance surveillance of diseases threats, but need to increase our support for building the workforce of epidemiologists and other public health specialties that are vital to preventing, identifying and containing outbreaks. We also must ensure that we have the ability on the ground to reach at-risk populations with core public health interventions, such as communication strategies designed to mitigate the spread of disease and clearly define the risks of an emerging threat. This will pay dividends with more resilient communities

that are better prepared for a flu pandemic and can withstand, absorb, and adapt to other public health incidents before they become emergencies. Moreover, these investments require our continued attention and commitment over the long-term and should not depend solely on the occurrence of a public health emergency. Our experience with 2009 H1N1, and the lessons we have learned, demonstrate a need to examine new paradigms for leveraging the public health infrastructure and our healthcares systems to develop the needed capabilities to ensure every community is prepared to respond to and recover from future disasters.

Thank you for your time and interest. I am happy to answer any questions.

Mr. PALLONE. Thank you, Dr. Lurie.
Dr. Goodman.

TESTIMONY OF DR. JESSE GOODMAN

Dr. GOODMAN. Chairman Stupak, Chairman Pallone, and members of the subcommittee, I really appreciate the opportunity to be here today to describe FDA's activities in this response.

First, when this influenza virus emerged in the spring we said this can't be business as usual and we immediately set up an incident command system response with several teams, for example, in antivirals and vaccines. And this enabled us to mount a very flexible and rapid response with our partners inside and outside of government.

In vaccines, our vaccine team acted immediately along with CDC to begin the steps to produce a vaccine even before there was a decision or knowledge that we were going to need one.

As you heard, in record time vaccine was produced and became available, and I can assure you everyone in this effort, government and industry, has done everything possible to get as much vaccine to as many people as quickly as possible without cutting corners. And I know this committee is concerned that a vaccine be safe.

A very important perspective here is that the entire world is struggling with the biology of this virus, the challenge of reduced manufacturing yields, and frankly the entire world is struggling with inadequate vaccine manufacturing infrastructure.

Yet despite these challenges we face in the United States and the frustration we have been talking about, this country is one of the first to mount an effective large scale immunization campaign.

Now, many people have asked us at the FDA how can we be confident in a vaccine produced so quickly. We have this paradoxical situation where many people really want vaccine and many people don't trust it.

Well, I would like to say that the answer is straightforward and to reassure the American people. The vaccines we've approved are made with methods that are tried and true. Every year FDA and vaccine manufacturers follow a series of very specific careful steps to produce new influenza vaccines every single year, and these steps have produced safe vaccines year after year, adding up to hundreds of millions of doses manufactured and used in the United States. And we followed this exact same scientific and regulatory approach for this 2009 H1N1 vaccine.

In response to some of the disinformation that was mentioned, I think by Congresswoman Castor, one of the things we have done, for example, is my Commissioner, Dr. Hamburg, with our working together, sent a letter to every physician in the United States to explain about the vaccine, how it was produced, and to provide a balanced review of the benefits and risks of the vaccine. But clearly we have a lot more work to do there.

You heard from the others that your investments in pandemic preparedness have been critically important. With respect to domestic capacity, I want to say that in May FDA in an accelerated manner licensed an additional facility at Sanofi-Pasteur in Swiftwater that the company has said has dramatically increased

its ability to produce vaccine and that is helping us now so that's important. But clearly we have much, much more to do.

I would also say during this response we have worked with HHS to bring online multiple additional filling lines to help make sure we can get the vaccine that's produced out there as quickly as possible.

Now, on September 15th we licensed four vaccines against the influenza virus, a fifth last week, and I also wanted to point out that again in a very collaborative effort with the CSL manufacturer who submitted data to us we were able to extend the approval of CSL's vaccine to include children down to 6 months of age who we are very concerned with.

Now, while we expect these vaccines to have the same excellent safety record as seasonable vaccine every year, we are taking nothing for granted. The same intensive oversight of these facilities, the enhanced safety monitoring Dr. Schuchat mentioned, and I want to point out that every single lot of vaccine must be evaluated, tested, and then released by both FDA and the manufacturer before it is used in people.

Now, because of the limited time I won't go into the work we have done on antivirals and diagnostics. I do want to say that we have prevented, for example, through emergency use authorizations discarding of antivirals that we scientifically know is safe to use, and that has helped avoid shortages. Diagnostics have been fielded in record time, within weeks of the new disease, thanks to CDC's effort and our work with them collaborating to evaluate those.

You've heard about protecting the public from fraudulent and counterfeit products. We almost immediately put a team in place to surf the Internet, to deal with consumer complaints. My favorite is the magic wand that can protect against everything, including anthrax and H1N1. But you also heard there are issues of counterfeit and unapproved medications. We are continuing to be very vigilant in this respect, and we have actually put a widget out there so others can spread the word with the list of counterfeit products.

Now, looking ahead, I really do feel much has been accomplished in a very short time, and it is because of these strong collaborative efforts that the people you are seeing here and many more are talking every single day. We are talking with the States, we are talking with the manufacturers, and this has been going on from day one. But we need to ask ourselves, and we are asking ourselves, what do we need to do more both right now for this epidemic and moving forward.

Clearly you've heard about we need more capacity, we need cell-based manufacturing, and we at FDA are very committed to make that happen. We recently last year or the year before provided guidance so we could get cell-based vaccines, but we also want those to be safe. We are supporting with HHS development of recombinant and newer technologies that can help us respond even faster. And I think, as I heard from one member, this is important not just about flu, this is important about other emerging infectious diseases. If we had SARS, if we had a bioterrorist attack, we need a strong technologically advanced vaccine infrastructure.

Now, due to time I think I will stop there, but just to say that we at FDA are very committed to working with our partners and you to protect the health of the American people. We've moved forward with a very flexible rapid response while taking our responsibility about the safety of these products very seriously. We really want to encourage strengthening our infrastructure here.

I also want to mention again that this is a global issue, and we in the United States can work with global partners to strengthen the global response. None of us are safe and well protected from infectious diseases until we all are.

So I thank you for your support for public health, your support for the FDA, and your interest in this issue. Thank you very much.

[The prepared statement of Dr. Goodman follows:]

Testimony before the
Subcommittees on Health, and Oversight and Investigations
Committee on Energy and Commerce
U.S. House of Representatives

H1N1 Preparedness: An Overview of Vaccine Production and Distribution

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INTRODUCTION

Chairman Stupak, Chairman Pallone, and Members of the Subcommittees, I am Dr. Jesse L. Goodman, Chief Scientist and Deputy Commissioner for Science and Public Health (Acting) at the Food and Drug Administration (FDA or the Agency). I appreciate the opportunity to be here today to describe the role of FDA in our nation's response to the H1N1 influenza pandemic.

When the 2009 H1N1 influenza virus emerged in the spring, FDA established an incident command system to speed and coordinate our response and to facilitate collaboration with and outreach to our external partners. The Agency created teams to address vaccines, antivirals, diagnostics, personal protection, and consumer protection.

This approach allowed us to work hand in hand with our sister agencies within the Department of Health and Human Services (HHS), including the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the Office of the Assistant Secretary for Preparedness and Response (ASPR), as well as other offices and colleagues within the Department, to help rapidly mobilize the public health emergency response. I am pleased to provide updates in each major area of FDA activity, as well as the challenges of the present and future.

Vaccines

FDA's vaccine team has worked with our sister HHS agencies, other U.S. government agencies, the World Health Organization (WHO), foreign governments, sister regulatory agencies, and vaccine manufacturers to facilitate the development, production, and availability of safe and effective vaccines against the 2009 H1N1 virus. While vaccines were made, licensed, and delivered to people in record time, the amounts of vaccine available to date are substantially less than had been expected, primarily because the virus is not growing as well or yielding as much vaccine as forecast. While we are frustrated that more vaccine is not now already available, everyone engaged in this effort—government and industry—has done and is doing everything possible to get as much vaccine to people as quickly as possible and to help close the gap between demand and supply. This includes continuing to work with the HHS Office of the Assistant Secretary for Preparedness and Response's (ASPR) Biomedical Advanced Research and Development Authority (BARDA) and with manufacturers to successfully increase vaccine yield as well as production capacity including, for example, bringing on board several additional manufacturing lines to fill and finish vaccine. These and other collaborative efforts have helped the continuing increase in vaccine production and availability. An important perspective is that the entire world is struggling with the biology of this virus and the challenge of reduced manufacturing yields and that the United States, thanks to a rapid response and public-private collaboration, has been one of the first countries to mount an immunization campaign with substantial availability of millions of vaccine doses.

At the same time that many are seeking the vaccine, and as more individuals are immunized, many people have asked how FDA and the scientific community can have confidence in a vaccine produced so quickly for a disease so new. The answer is straightforward: the vaccines

FDA has approved are made with methods that are tried and true. These methods rest on a strong scientific foundation and a tremendous amount of experience. Each year, FDA and vaccine manufacturers follow a series of steps to make a new influenza vaccine targeted to the three main circulating strains of influenza. These steps have produced a very safe vaccine time and again, adding up to hundreds of millions of doses administered in the United States. We followed this same scientific and regulatory approach for the 2009 H1N1 vaccine. Throughout all of this effort, FDA, CDC, NIH, ASPR, and vaccine manufacturers have worked together intensively to do all that is possible to speed vaccine production and availability.

I will briefly summarize each of the key steps.

First, within weeks of the very first cases appearing in April scientists modified the 2009 H1N1 virus into versions suitable for producing a vaccine. For each year's seasonal influenza vaccine, this step is an ongoing process that occurs in laboratories around the world, including FDA's, in conjunction with surveillance to identify new influenza virus strains that might pose a public health threat. For the 2009 H1N1 virus, strains needed for vaccine manufacturing were created and provided to manufacturers by early summer 2009.

Second, companies began to grow the vaccine strain in specially produced chicken eggs. As recently as a few years ago, eggs would not have been available in the summer, and vaccine production would have been substantially delayed. Fortunately, this year, thanks to your support and the investments by HHS in pandemic preparedness, manufacturers immediately could tap into a reserve supply of eggs made by additional flocks of chickens. These flocks were available under contracts put in place by ASPR for just this purpose—to prepare to respond to a possible

pandemic. To incubate the eggs and make vaccine, companies used facilities specifically inspected and licensed by FDA for influenza vaccine production.

Similarly, investments in pandemic preparedness by Congress and work by ASPR and FDA mean that we have more licensed manufacturers and more production capacity. For example, in May, FDA licensed additional manufacturing capacity at Sanofi Pasteur's Swiftwater, Pennsylvania, facility: capacity that is now playing an important role in providing vaccine to our nation. While we clearly need much more capacity in both the United States and globally, without the investments of the past several years, and our ongoing efforts, the current situation would be far more challenging.

Third, we sought outside input from experts and the public. At the end of July, FDA convened a public meeting of its expert vaccine advisory committee to review the Agency's approach to approval of the 2009 H1N1 vaccines. This committee includes scientists, physicians, public health officials, and a consumer representative. The committee supported making the vaccines the same way and holding them to the same standards used every year for the seasonal influenza vaccine.

Fourth, we developed and then provided manufacturers with reagents and tests needed to measure the vaccine's potency—a step essential in manufacturing. Scientists from the United States, United Kingdom, Australia, Japan, and other nations, working together with WHO, developed these tests to assure the proper amount of influenza antigen goes into each dose of vaccine to induce an antibody response, thus providing protection against disease caused by strains included in the vaccine. This is an essential step before final vaccine production can be completed.

On September 15, after reviewing applications from manufacturers similar to those submitted each year for licensed seasonal vaccine, FDA licensed four vaccines against the 2009 H1N1 influenza virus. A fifth vaccine was licensed last week. FDA found that all of the standards to ensure the safety and potency of these vaccines had been met.

Over the summer, NIH and vaccine manufacturers initiated clinical trials to determine the optimal dosage and number of doses needed to induce a protective immune response. These trials have helped both the U.S. and the world understand H1N1 vaccines and how best to use them. Just as for seasonal vaccine, one dose of unadjuvanted H1N1 vaccine induces a robust immune response likely to be protective for adults and older children. For younger children, two doses of the H1N1 vaccine will likely be optimal, also as seen with seasonal vaccines. No serious safety problems attributable to the vaccine have emerged during the trials, which have so far included over 3,600 subjects at NIH-supported institutions alone.

We are not taking anything for granted. We subject the 2009 H1N1 influenza vaccines to the same stringent manufacturing and quality oversight processes that are in place for seasonal influenza vaccine. FDA inspects these plants at least once a year to assure that quality controls are followed at every step in the production process. Each facility also is inspected annually for compliance with FDA's current Good Manufacturing Practices. Extensive in-process quality control and product testing (such as for potency and purity) are required at multiple stages of the manufacturing process. No lot of the 2009 H1N1 vaccine can be used until it has been fully tested and released as sterile and potent by both the manufacturer and by FDA. While we expect these vaccines to have the same excellent safety profile as seasonal influenza vaccines, CDC and FDA are collaborating with both multiple U.S. partners and our global counterparts to build a

markedly enhanced safety monitoring system that utilizes data available across U.S. Government agencies and in the health care system, as well as globally, to look for any unexpected, rare, serious adverse events and to quickly investigate concerns. Should any safety concerns arise, we will evaluate them thoroughly and bring them quickly to public attention. Again, collaboration across the public and private sector has been unprecedented. These efforts also will strengthen and inform future safety monitoring efforts for vaccines as well as other products

Antiviral Products

An effective response to H1N1 must involve a full range of prevention and treatment. FDA's antiviral team has worked hard to facilitate the availability of antiviral medications for ill patients in the United States. Fortunately, to date, the 2009 H1N1 virus has generally been sensitive to the FDA-approved antiviral drugs, Tamiflu® and Relenza®. On April 27, 2009, FDA issued two Emergency Use Authorizations (EUAs) that authorize additional circumstances in which those medicines can be used to treat illness caused by the 2009 H1N1 influenza virus. These authorizations were utilized by CDC and state and local partners to speed and extend access to these medications to patients in need of treatment all over the country. FDA's work on dosing of Tamiflu in children less than 1 year of age was adopted by countries around the world. Since that time, the antiviral team has worked to authorize the use of needed antiviral drugs through several creative and effective public health actions.

FDA has worked with ASPR and with manufacturers to do everything possible to speed additional production of Tamiflu and Relenza. The public/private interaction has been very positive and manufacturing continues at high volume. All current manufacturing capacity is

being fully utilized and, as has been the case for vaccine production, FDA stands ready to perform priority review of any additional manufacturing capacity industry can bring on line.

FDA determined through scientific review and analysis of available data by FDA scientists that certain lots of Tamiflu and Relenza can be safe and effective when used beyond their expiration dates. As a result, for this emergency, FDA authorized the appropriate use of large amounts of antiviral medications that may otherwise have been thrown away because it was beyond its labeled expiration dates, thus helping prevent shortages and keeping needed medicines available for patients. FDA also recently extended this EUA authorization to include these drugs in the possession of the private sector, keeping businesses and health care delivery systems around the country from having to throw out medication that FDA has determined is still acceptable for use beyond its expiration dates.

While Tamiflu capsules and inhaled Relenza remain in good supply, in part due to these measures, we also recognized the potential for shortages of Tamiflu and Relenza products, particularly of the Tamiflu for Oral Suspension (liquid Tamiflu used to treat young children who cannot swallow pills). Working with manufacturers, we provided guidance for pharmacists to enable them to mix Tamiflu from capsules with syrups, to make a compounded version of liquid product for children under emergency circumstances, when supplies of oral suspension are otherwise unavailable. Since the emergence of the 2009 H1N1 influenza virus, FDA and CDC have worked together to provide a series of outreach communications to help ensure that pharmacies are familiar with this option. Many pharmacies large and small, including major chains, such as Walmart and Walgreens, have stepped up to meet this need, and their pharmacists

will make a liquid Tamiflu formulation, as needed. Recently, after receiving suggestions from our partners, FDA updated its communications to make the compounding process more efficient in situations where multiple prescriptions are being filled.

Further, FDA has closely tracked shortage reports for antiviral drugs, working with the medical community and hospitals to identify areas that are in greatest need of supplies. Currently, there are no approved intravenous influenza antiviral medications. Access to intravenous antivirals is extremely important for critically ill patients who may not be able to take or absorb oral or inhaled dosing forms, or in whom intravenous administration is the only dependable route. ASPR has been supporting the development and production of intravenous antiviral medicines to help meet this need. These include peramivir, a medication similar to Tamiflu in how it keeps the influenza virus from growing. Peramivir is not yet an approved drug and is still undergoing assessment of its safety and effectiveness in clinical trials. On October 23, 2009, working closely with CDC, and after careful evaluation of available data from clinical studies to date and from emergency treatment, FDA issued an EUA for peramivir intravenous (IV), facilitating its use and availability to appropriately treat certain adult and pediatric patients with confirmed or suspected 2009 H1N1 influenza infection who are admitted to a hospital.

In Vitro Diagnostics

When the outbreak began, there were no laboratory tests available that could accurately diagnose infection with the 2009 H1N1 virus. Existing rapid influenza tests are not reliable for this H1N1 virus, and to date no test has been cleared or approved for the diagnosis of 2009 H1N1 influenza virus. CDC mobilized quickly to produce a test for use in laboratories with suitable expertise, and FDA worked with CDC to rapidly evaluate the test and issued an EUA on April 27, 2009,

making testing available to a wide network of public health and other qualified laboratories very soon after the start of the outbreak, a remarkable accomplishment. Since that time, FDA has worked with others in both government and the private sector to increase the availability of reliable testing for 2009 H1N1 influenza under EUAs. Nine EUAs have been issued for H1N1 laboratory tests, including one to the Department of Defense on August 24, 2009, using rugged equipment that allows for testing in remote areas including near combat. Recently FDA published guidance intended to provide information on the types of data developers should submit in a request for an EUA for a test intended to diagnose H1N1.

Personal Protective and Other Medical Equipment

FDA has worked with CDC, ASPR, manufacturers, and others to increase production and availability of personal protective equipment such as gloves, masks and respirators, and to enhance the supply chain of equipment needed for respiratory and intensive care. On April 27 of this year, FDA authorized an EUA for 15 different N95 disposable respirators, allowing for emergency use of these respirators in our national stockpile.

Protecting the Public from Fraudulent Products

Unfortunately, many people are seizing on the 2009 H1N1 influenza pandemic as an opportunity to make fraudulent claims and promote fraudulent treatments to the public. Many of these deceptive products are being sold over the Internet through illegitimate Web sites, and prey on consumers' desires to protect themselves and their families. These products come in all varieties and include dietary supplements or other food products, as well as products purporting to be drugs, devices or vaccines that prevent or treat illness caused by the H1N1 virus. If vulnerable patients purchase these fraudulent products and delay or avoid treatment or vaccination, tragedy could result.

FDA anticipated these risks and established the 2009 H1N1 Consumer Protection Team that has put in place an aggressive strategy to combat fraudulent 2009 H1N1 products. It has been active in protecting the public by identifying fraudulent products and following up with enforcement actions, as appropriate. The team has sent over 75 official warnings to more than 80 Web sites, covering about 140 different products, and has given Web site owners 48 hours to respond. Currently, FDA's warnings have resulted in a compliance rate of 85 percent.

Since May 2009, the Agency has issued four press releases to alert the public about fraudulent products. Fraudulent products targeted and subject to warnings from FDA, range from shampoos, soaps, solutions, and sprays claiming to be scientifically proven to kill the 2009 H1N1 influenza virus—to power immune drops that claim to exterminate the virus from one's body—to a test that claims it can detect the virus—to products that claim to be safer, more effective, natural alternatives to the 2009 H1N1 influenza vaccine. Products purporting to be Tamiflu or other antiviral drugs may be contaminated, contain impure, unknown, or ineffective ingredients, or only contain aspirin.

The nature of the Internet means that often, as soon as one site comes down, another replaces it. We know that as long as public health threats exist, there will be those who will try to exploit the fears of consumers. The public should know that if a product seems too good to be true, it probably is. To help, we have put an easily accessible list of fraudulent products on our Web site as well as provided a widget that anyone can download to their own Web site to help spread the word. We will remain vigilant and ask consumers to do the same.

Looking Ahead

Much has been accomplished in a very short time by the strong collaborative efforts of those working inside and outside our government. While we are facing this public health challenge, we should ask and are asking ourselves, even in the midst of it, what can we learn to do better, both now, as we respond, and for the future?

First, even though the first vaccines became available quickly, using tried and true egg-based technologies, we need much more capacity, both in the United States and globally, to produce them. In the United States, major investments are underway in advanced vaccine development and manufacturing capacities, which include vaccines manufactured in cell culture systems. FDA has provided guidance to manufacturers to help ensure that cell culture-based vaccines can be made safely. In addition, we are supporting the development and use of recombinant and other newer technologies that offer the potential to serve as "platforms" for more rapid development, production, and deployment of vaccines against new influenza viruses or other emerging public health threats. These approaches may offer a number of advantages in scalability, reliability and speed. Such efforts are ongoing and, with your support, must both continue and be augmented.

Second, HHS is funding the development and careful evaluation of adjuvanted influenza vaccines. Adjuvants are substances added to vaccines that are intended to help boost the immune response. There are instances in which adjuvanted influenza vaccines may be needed or desirable, for example, when the vaccine cannot induce an adequate protective immune response without them, or to potentially help broaden the immune response to address dramatic shifts in strains that might occur as an outbreak evolves. Currently FDA-licensed influenza vaccines do not contain adjuvants. However, both NIH-based and HHS-supported industry-based studies are

underway, including with the 2009 H1N1 virus, that are increasing the information available on the safety and effectiveness of these products, and that are informing their evaluation. Adjuvants have been purchased and stockpiled in case they are needed for use under an EUA during the current emergency. Fortunately, as noted, studies to date show that currently approved standard doses of nonadjuvanted licensed vaccines induce an excellent immune response expected to be protective against the 2009 H1N1 virus, which has remained very stable to date.

Third, we need more modern tools to assess influenza vaccines and to speed their production. At FDA's laboratories, and in collaboration with colleagues at CDC, NIH and globally, scientists are researching ways to improve the assays, reagents, and tests needed to more rapidly and accurately evaluate, produce, and test the quality of current and future influenza vaccines. This work has the potential to expedite vaccine development and speed availability, and ensure vaccine quality, using the most modern scientific methods.

Fourth, ongoing scientific efforts at NIH and FDA are evaluating even more advanced approaches, such as DNA vaccines and "universal" influenza vaccines, which potentially may protect against multiple and evolving influenza strains.

Finally, influenza is truly a global problem requiring global collaboration. Although FDA is a WHO Collaborating Center for Influenza, and already participates in collaborative work and technical assistance through WHO and with regulatory agencies throughout the world, a much broader and deeper global collaborative effort to enhance the influenza vaccine infrastructure would be desirable and beneficial to both U.S. and global health.

Vaccines are only part of the picture. As we respond to this pandemic, we also should take the opportunity to learn from this novel virus and the public health response, in order to promote the development of needed antivirals (which would be critical if a resistant virus should emerge), rapid diagnostics, and enhanced safety surveillance capacities, and identify remaining scientific and public health questions. Our continued work, from basic and applied science to the medical products and public health interventions that may be used to protect people in the United States and around the world, will benefit us in preparing for and responding to biological threats, whether natural or man-made.

Conclusion

FDA is fully committed to and engaged in protecting the health of the public during this challenging time. Among us are laboratory scientists, epidemiologists, medical reviewers, product experts, and field inspectors. We will bring every skill and resource we have to this critical mission. The collaboration among U.S. Government agencies has been remarkable, and interactions with the private sector and global partners have been proactive, constructive, and essential in addressing the outbreak. I thank you for both your support for public health and for the opportunity to testify today and will be pleased to answer any questions from Members of the Subcommittees.

Mr. PALLONE. Thank you, Dr. Goodman, and thank you to all of you. The way we proceed now is we have a 5-minute period of questions from members going back and forth, Democrat, Republican. For members who passed on their opening they get 7 minutes. They get to add their opening to the 5. I'm going to start with myself. And I want to start with Dr. Schuchat.

The big concern—the biggest concern that I hear from my constituents is about the distribution. And I know that the CDC has guidelines for distribution, but basically leaves the distribution up to the States as long as they meet those guidelines. My concern is whether that's a good way to go about it. I mean I suppose you assume that the States and the localities, since they are closer to people, would have a better—would be the best way to distribute, but that's been seriously questioned in the last few months or so. And of course being from New Jersey the biggest issue has been the Wall Street companies; Goldman Sachs, Citigroup. I literally, being from New Jersey, hear about this constantly.

Why is it that New York, I guess you know, gave Goldman Sachs and Wall Street firms the opportunity to do this? I'm told that employer-based distribution is one of—meets your guidelines. And perhaps it was assumed that they would do well since they have health clinics and have a good distribution amongst their employees.

But I guess the concern would be, you know, if you leave the distribution to those who do it best and the ones that do it best happen to be, you know, high-powered Wall Street firms, then there are two concerns. One would be does that make sense given that maybe a hospital or a school might not do as well a job at distributing but there is a greater need.

And then the second thing is whether or not some of these firms would only give it to high risk people as opposed to maybe their CEOs or somebody else. So I mean that's the concern. I mean, my question really would be why does the CDC leave it up to the States to create the plan for distribution and wouldn't it perhaps be better to have some other Federal mechanism rather than doing it this way? And what, you know what prevents somebody like Goldman Sachs getting it when it maybe should be going to a clinic and monitoring how they go about it?

Dr. SCHUCHAT. Thank you. The CDC issues national standards about the populations at greatest risk for disease that are recommended to receive vaccine when there is a scarce situation. So we issue that as a national level setting. We leave it to the States or the large cities like New York City to find the best ways to put vaccine in the path of the priority populations, to identify the venues.

New York City actually put hospitals and doctors' offices first. They put employer clinics in a lower tier and small numbers of doses went to some employers——

Mr. PALLONE. But the problem that I'm hearing, you know, I don't have a lot of time, is that in some of those cases, I don't remember which Wall Street firm it was, they actually had excess and didn't need it. So you know you could argue that maybe they are getting fewer dosages but you know it may very well be that maybe all or most of what they got should have gone to the hos-

pitals because there is a greater high risk pool there. How do we prevent that?

Dr. SCHUCHAT. I think that issue was of concern to all of us. Dr. Freiden sent a letter out to all of the health officers reminding people about our priority groups and how critical it is for all of us to adhere to them. Every provider or venue that gets vaccine signs an agreement that they are going to follow the recommended target populations.

Mr. PALLONE. And I understand that—I'm not suggesting, although some have, that Goldman or others are giving it to people other than the high risk, although some are concerned about that. But it is just that have you thought about the fact that if you do it that way or if the States do it that way it may be giving it to people that have a better distribution network within their employers but they may not have as great a need? It is sort of like when there is a grant program and the guy that does the best, has the best grant application person gets the grant whereas maybe there is a greater need for the person who doesn't have an expert to do it, you know.

Dr. SCHUCHAT. We have had a major commitment to vulnerable populations and to the underserved and to make sure that we are not leaving behind those without good access. Most of the States have carried out these larger mass clinics to get people who do not have doctors' offices to go to.

Mr. PALLONE. If you can just—I don't know if you have it, but I would like to see, maybe get back to me at some point to talk about why this kind of distribution is better as opposed to maybe looking at some kind of a Federal alternative. I don't know to the extent that you've looked at that, but if you could get back to us at some point.

Dr. SCHUCHAT. Thank you.

Mr. PALLONE. And then the other thing I wanted to ask Dr. Lurie is that when Secretary Sebelius testified before the committee on September 15th, I mean basically she left us with the feeling that we are on track in terms of adequate supplies of vaccine. I know that turned out not to be the case, some of you explained why and I'm sure we will get more questions from the other panel. But you did mention underfunding, and I don't remember her saying anything about lack of funding. You said that underfunding or chronic underfunding was one of the contributing factors. That's the first time I have heard that, and I was a little disturbed because I don't remember her mentioning it.

Dr. LURIE. Let me try to clarify here. I think the chronic underfunding has been in the vaccine infrastructure overall, as opposed to the response. So it would have been wonderful if we had had more manufacturing capacity in the United States by this point, if we had had cell-based or recombinant technologies that could surge and really produce large amounts of vaccine.

But, you know, while we have invested in that over the past few years, we need to continue to make a much more robust investment. So that is the kind of chronic underfunding for the vaccine manufacturing capacities.

I think we all know that the chronic underfunding in State and local public health has been a different kind of problem. But Con-

gress has been extraordinarily responsive to the very acute needs that we have had to deal with in this pandemic, and what I would like to see us in the situation of is that we can sort of apply prevention in that sense too and really get ahead of this for the next pandemic.

Mr. PALLONE. Again, as I said, I don't want to beat you guys up today, but when it is something like that that Congress can make a difference, it really is important that if the Department or anybody feels that there is a need for more funding, to detail that to us.

Again, I would ask you maybe to get back and give us more information about this chronic underfunding in writing, because a lot of things that come up here, we can't do anything about. But that is certainly something we could.

Dr. LURIE. We look forward to working with you on that.

Mr. PALLONE. Thank you.

Mr. Walden.

Mr. WALDEN. Thank you very much, Mr. Chairman.

Dr. Lurie, thank you, and thank you all for your testimony.

I note Secretary Sebelius did state in retrospect that the vaccine manufacturers had painted a "rosy" picture. Now, some of you have indicated you have been in contact almost on a daily basis with these same manufacturers. My understanding is the seed that they used to produce this vaccine was made available to them on June 23rd. We had testimony September 15th from Secretary Sebelius saying everything seemed to be on track and fine.

So explain, did the manufacturers, weren't they straight with you? What is this rosy picture piece? Is that blaming the manufacturers?

Dr. LURIE. I don't think there is anybody to blame here. I don't think that there is a smoking gun, and I want to make that really clear. It is a very complicated process.

What we have tried to do is put together a little graphic here that shows you all of the different points where things can break down. So I think in the very beginning when we had that seed strain and started making vaccine, everybody was very optimistic. Nobody anticipated how hard it was going to be to get this thing to grow. Manufacturers got a new seed, they started having increases in their yields.

Mr. WALDEN. I don't mean to cut you off, but they only give us 5 minutes here to solve the whole vaccination issue.

When did you first learn vaccine production was going to be delayed?

Dr. LURIE. Well, what I should say is we learned at several points along the way. We learned over the summer that there were problems with this vaccine growing. We learned in the fall that there were problems——

Mr. WALDEN. My understanding on that is that regular vaccine or the traditional flu vaccine would produce about 3 doses per egg, and this was producing like a tenth of a dose or something?

Dr. LURIE. Somewhere between .2 to .5 or something. So that was very challenging. What I will say is at every step along the way when we got information that things were not going as quickly

as possible, we actually downgraded our estimates and we got that information out to the American public as quickly as possible.

Mr. WALDEN. I guess what we are trying to get at here is I was here for that hearing on September 15th, and I walked away thinking, wow, that is a pretty strong statement, to say we are going to have vaccine for everybody on schedule on time and 20 million doses in October, or whatever the number was, and then we got people waiting in line for hours. I mean, people are really frustrated.

Dr. LURIE. I think we are all really frustrated. I don't have any doubt about that.

Mr. WALDEN. But did the Secretary know when she testified in September of these delays?

Dr. LURIE. When she testified in September, those initial getting-the-virus-to-grow problems had been largely cleared out of the way. Then, you know, as happens, other problems happened. Problems in getting production lines up and running, for example, just took longer than they could have, so it actually took longer to get from the big vats of vaccine into vials that you could actually ship out to States, just as another kind of example. And at every step along the way. Even now we still have problems. You know, if a dose gets shipped here and a temperature sensor goes off, or like the storm, things happen.

So at every step of the way things happened. When the Secretary testified, she was using the best available information she had at the time.

Mr. WALDEN. Let me move on to a different topic then, because one of my colleagues who had to leave wanted me to ask if we could have for the committee the contracts you entered into with the manufacturers, if we could? Is that something you can provide?

Dr. LURIE. Absolutely.

Mr. WALDEN. And one of the questions that has come up is in the contracts, did the manufacturers or did you request knowledge as to whether or not these offshore manufacturers, which is all but one, I understand, that their countries, like we have the authority, can say, produce the drugs for us first and then you can ship to the U.S.?

Was that discussed with each of these manufacturers, and did HHS know ahead of time kind of where we might get a manufacturer that is required by their in-country law to provide the vaccine there first, and we might have been relying on that shipment here? Did that pose problems that we know?

Dr. LURIE. Let me say first that these contracts are all structured so that manufacturers don't get paid until they produce vaccine. I just want to make that clear, because I think that there has been a lot of confusion about that. We have worked very hard to be responsible stewards of society's resources in that respect.

Yes, almost every country has what this country has——

Mr. WALDEN. So you knew going in.

Dr. LURIE. Going in, or early on into this, we did know that other countries had this.

I also want to just say that despite the problem in Australia, CSL has worked very, very hard to get us vaccine as soon as it got freed up.

Mr. WALDEN. I understand. The final question, because it is, I believe, in your testimony, is your reference to this vaccination team that has been sent to Delaware. What is that about and why Delaware, other than maybe the Vice President's home?

Dr. LURIE. Because they requested it. So one of the things that we did in working with our colleagues at CDC and State and local health departments is we said we want to do everything we can to help everybody be successful and get vaccinators out there. So if, within your State, you don't think you can mobilize the resources to get populations vaccinated, we actually through the National Disaster Medical System have trained about 15 teams now that on request could go out and help gets those vaccines into arms and noses. There is one out there, I think next week, to help college kids.

Mr. WALDEN. Are there other States requesting that, and how do they do that?

Dr. SCHUCHAT. Just to add that CDC has also received requests and we have adapted. So Dr. Lurie is describing one mechanism. CDC has got other mechanisms. But everybody's shared goal is to support the States in succeeding.

Mr. WALDEN. That is terrific. So those vaccination teams are available through HHS, limited numbers, and States can apply, and you are communicating, I assume, with our governors on you how they can do that?

Dr. LURIE. Yes, we are.

Mr. WALDEN. Thanks for your indulgence, Mr. Chairman.

Mr. PALLONE. Chairman Stupak.

Mr. STUPAK. Thank you, Chairman Pallone.

Let me ask a couple of questions because I am a little confused on a couple of things. What I have heard everyone say, or Dr. Schuchat, you said next time we will have more time, we will have more vaccines, we have learned.

Dr. Lurie, you said we have gathered data from around the world and the H1N1 has not mutated significantly since the spring and we are doing what other countries do. And Dr. Goodman, you said the entire world is struggling with the biology of this virus and that you worked with foreign governments and the World Health Organization.

Can you show Exhibit 4 for me.

When I was looking at this, HHS has put out a timeline, the 2009 H1N1 activity timeline, and I noticed the antivirals was very important, the page I looked at. On the antivirals here, I saw here on April 28th HHS released its 11 million treatment courses, 25 percent of the Federal antiviral stockpile held in the Strategic National Stockpile to States in anticipation of State influenza efforts. The Secretary approves a procurement of 13 million treatment courses to replenish those to the States and Mexico.

We know it heart started in Mexico, at least on this side of North America, and this was in the spring. Mexico was having trouble. We sent them 13 million treatments. April 30th, HHS provides 400 treatment courses, one percent of the Nation's stockpile to Mexico to help spread the virus. And I have no problem with doing that.

But what did we learn from all these countries? Because it seems like the problems, and we had supply to help out Mexico, that,

number one, there was a shortfall. Number two, we are trying to come up with vaccine formulary. Number three, does only one dose work or do we need two doses? And four, what about the young people, especially the pediatric deaths seen in this county? Didn't we see that, all the same things in Mexico? Go ahead.

Dr. SCHUCHAT. I can probably begin and let others finish. We have worked very closely with the global community to learn as much as possible about the behavior of the virus in people everywhere, particularly with——

Mr. STUPAK. How about these questions? Did we realize there would be a shortfall from at looking at Mexico, did we find a vaccine formulary, did we realize only one dose would work, and the young people being injured. Didn't we learn that from Mexico and working with the other countries?

Dr. SCHUCHAT. One dose seems to work in children 10 and adults.

Mr. STUPAK. My question is, did we learn this in April from working with other countries?

Dr. SCHUCHAT. No, there was no vaccine in April.

Mr. STUPAK. Why did you ship it to Mexico then if there is no vaccine?

Dr. SCHUCHAT. No, we shipped antivirals to help them, because they had people dying in hospitals.

Mr. STUPAK. Yes, they had people dying in Mexico. So what did we learn from that?

Dr. SCHUCHAT. We learned that the clinical severity in Mexico is very similar to here. Their initial reports of very severe disease were because they hadn't actual looked broader in the community. They found a lot more mild disease once they started looking. So we learned that the clinical picture in Mexico turned out just the same as what we have had, the same in Australia, the same really around the world.

Mr. STUPAK. So then it still took us 6 months after shipping to Mexico and everything else to learn, number one, we are going to have a shortfall; number two, that we didn't release the license to these manufacturers until September 15th; we didn't realize we needed only one dose, according to your timeline until September 11th; and that young people were going to die.

Dr. SCHUCHAT. Right. The vaccine clinical trials were carried out during the summer, and so decisions on licensure were based on product submissions to the FDA.

Mr. STUPAK. Let me go to this question then. If we are having all these problems, we know there is these shortfalls, all this is going on, and you have your emergency use authorization, then this adjuvant, are we the only country that doesn't require an adjuvant, that we said no adjuvant? If we are learning from all the rest of the countries, other countries aren't using adjuvant, why are we insisting—we are non-use, right?

Dr. SCHUCHAT. We are not using adjuvant.

Mr. STUPAK. Other countries are using adjuvant, right?

Dr. SCHUCHAT. Some are using adjuvant.

Mr. STUPAK. Why aren't we? Especially when our suppliers are telling us we can quadruple the amount of vaccines available if we would have used it when we realized we have all these short sup-

plies, and you have an emergency authorization, emergency use authorization, and the President issued a national disaster declaration on October 24th. So you are looking at the rest of the world, Novartis and some of the other manufacturers tell us, look, we can quadruple your supply just by using the adjuvant, and we say no, we are not going to do it.

Dr. LURIE. Let me see if I can sneak in, and maybe Dr. Goodman would also like to comment. Adjuvants haven't been licensed in the United States. We haven't had a lot of experience with them.

Mr. STUPAK. Correct, but the rest of the world has.

Dr. LURIE. Their safety profile was not known, and so we got all of our top scientists together and we made a decision that if the situation got a lot worse, then we would use adjuvants.

Mr. STUPAK. How much worse does it have to be before we use adjuvants?

Dr. LURIE. We also thought since the unadjuvanted vaccine also worked quite well, that that was a better alternative.

Mr. STUPAK. But we receive 25 percent less than what we could have if we used the adjuvant. What is the problem with the adjuvant, other than we haven't done the tests here in this country?

Dr. LURIE. Well, as you know, the public's confidence in our vaccine system and in vaccines in this country is very, very fragile. We made a commitment not to cut corners and to use vaccine that had been demonstrated to be safe and effective.

Mr. STUPAK. But it seems like we rely upon data from the rest of the world when it is our convenience, but then yet when we look at the track record of the rest of the world and this adjuvant, whether or not we add or not, suddenly we decide to go different. The M–59 adjuvant that Novartis talks about says look. The rest of the world, they had to change because the United States told them to change the formulary. So were we taking into concerns the needs of other people, or just our own people based upon our own interests? Then we could have had more supply out there if we would have looked at what Novartis and others say works.

Dr. SCHUCHAT. You know, one thing you may not be aware of is that the demand for the vaccine is actually much higher here than it is in Europe, and there is quite a bit of skepticism in Europe. So I think we have a very complex environment.

Mr. STUPAK. I agree. We hit it a little quicker than Europe. Europe may hit it here pretty quick, right?

Dr. SCHUCHAT. Absolutely. But I think the other point is, as Dr. Lurie says, at several steps since last spring, the government has reevaluated the adjuvant decision. We have looked to our external advisory groups. We have considered is this a scenario where it makes sense? And we don't feel that we have reached that point, given where we are with production.

Mr. STUPAK. OK.

Dr. GOODMAN. Chairman Stupak, maybe I can add one thing that may be helpful to you. One is that we are working very hard with the manufacturers. In fact, we have asked NIH and the manufacturers to study these adjuvants, including with H1N1, to give us more data.

The other point I wanted to make is that the vaccine you mentioned, that is marketed in Europe, so there is one previously ap-

proved adjuvanted flu vaccine in Europe. However, that was only previously approved for the elderly. So in terms of the kind of broad experience with millions of people, that is only in the elderly, who were not a focus population for this vaccine.

Finally, I do want to point out that it is not those identical vaccines that would be available here for our citizens, but vaccines where the vaccine material itself is manufactured in other facilities and then combined with those adjuvants, and there is much less information about that combination. And, again, that is why it is important for NIH and the manufacturers who have been very cooperative to provide this information.

So we don't have enough data about those at this point or at the beginning of the pandemic for them to meet the standard of FDA licensure. However, we have said all along, and the senior scientists at every agency at a scientific level are meeting periodically and reassessing this decision. In fact, a decision was made to go ahead and stockpile adjuvants and have them ready if they are needed. The good news has been that the normal doses of non-adjuvanted vaccine have induced an excellent response, just like every year.

Mr. STUPAK. But if you are stockpiling to determine if they are going to be needed what is the breaking point when you determine they are needed, if you already stockpiled it and it can give you four times more vaccine?

Dr. GOODMAN. Yes. I think that initially, for example, exactly what you are asking, a break, a breaking point would have been if a normal does didn't give a good response. Another breaking point would be if the virus changed dramatically and it looked like an adjuvanted vaccine could provide better protection.

But I think we are very open to this, and we have really tried to walk a line based on the science. It is very complex science, and we look forward to getting more information, and we are committed to continuing to assess it going forward.

Dr. LURIE. Let me just add that——

Mr. STUPAK. One minute. He has been generous with the time. I am way over. And the next panel is coming up I am going to ask them the same questions.

I still think we could have quadrupled our supply and taken care of our supply if we weren't so shortsighted in this.

Mr. PALLONE. Thank you.

We have 8 minutes left. We have three votes. Mr. Shimkus says he would like to go next before we break and then after him, we will break and come back.

Mr. SHIMKUS. Thank you, Mr. Chairman. I am just going to be pretty short. But I appreciate Bart's focus, because in my opening statement, I hope that we do an after-action review on this process to help us be prepared, because the questions that he is raising are really the questions that I would have under a terrorist attack, biological or weapons of mass destruction. And it really keys in to what Bart has said.

We have to have a way to streamline the process and get approvals quickly, and that would be the debate on egg versus cell and how quickly—I understand the FDA's responsibility. But if you

have a massive possible pandemic, we better have a way to subvert the regular order for the needs of the whole and move rapidly.

Just like Bart's comments on the adjuvant. I hope there is a process in place, and if there is not one, I am former military and after every training exercise you do an after-action review. Will that be done, Dr. Schuchat?

Dr. SCHUCHAT. What I can say is we have actually had several in-process reviews already, and we are committed to after-action reviews as part of our routine procedures.

Mr. SHIMKUS. Dr. Lurie?

Dr. LURIE. I would add to that, and I would also add that there are processes in place now through emergency use authorizations so that if this pandemic were to become much more severe, et cetera, we would be able to shift to other products under an emergency use authorization, and that has been part of our pandemic planning since 2005.

Mr. SHIMKUS. Because if something hits that we don't even know about and we are looking at this timeline, then I guess we just identify it and then isolate people until we can roll out, you know, some——

Dr. SCHUCHAT. There are several mitigation steps, and one of the things we did this summer was update guidance for mitigation, what to do with the current level of severity and what we might do if the virus mutated and was much more severe. So no automatic school closures in this setting, but if things changed substantially, we would go to much more disruptive interventions. So we do have things that were available to us, knowing that vaccine supply might not come soon enough.

Dr. GOODMAN. I really appreciate your comments, and we want to have a very agile public health response, especially in an emergency. I do want to mention that in that respect, it took us about a day or two when there was a need for antiviral, not approved for children under 1-year old, but to treat children under 1-year old, to work with our colleagues at NIH and CDC and issue an emergency use authorization. Full transparency to the public. Not the kind of data required for approval, but appropriate risk-benefit weighing and a public health response.

This is a tool you in Congress have given us, and we are ready to use it when there is the right emergency. And as recently as the last couple of weeks with respect to the adjuvant question, the senior scientists of every agency have sat together and revisited that decision and decided, do we want at this point to switch to adjuvants? It is a very complex discussion. But that is being revisited in action and we are committed to continuing to revisit it after action.

The biggest improvements we can make are strengthening this infrastructure and getting new technologies ready ahead of time. We are better prepared than we were a few years ago, thanks to your investment, but we have a long way to go.

Mr. SHIMKUS. And I will just end by saying I think education is a key. The positive aspect is the public is really better stewards of everybody else's public health by better health practices, and that will be the key thing before we can roll into this.

Thank you, Mr. Chairman, for letting me get this in.

Mr. PALLONE. Thank you, sir. We have three votes and we will come right back after that. The subcommittee is in recess.

[Recess.]

Mr. PALLONE. The subcommittee will reconvene.

Our next member is the gentlewoman from Wisconsin, Ms. Baldwin.

Ms. BALDWIN. Thank you, Mr. Chairman.

I mentioned in my opening statement three topics that I hoped to hear more on. I know that I won't get a chance to exhaust those three topics in Q and A, but let me start with Dr. Lurie on the issue generally of domestic production of vaccine.

You had been asked a question by Mr. Walden that I think time didn't permit you to finish answering regarding the policies in other countries where vaccine is manufactured, and I wondered if you could basically generalize those policies, but also tell us specifically what happened in the case in Australia?

Dr. LURIE. Sure. I think many countries, including the United States, in the United States we have the Defense Production Act, and basically what that tells us is that if we need material for the safety and security of this country, that we can prioritize that. And I think many countries have that kind of situation that they need to prioritize for their home country.

That is why it is so important for us to get to domestic manufacturing capacity in the United States. It is actually something that we learned and realized during our pandemic planning early on, and in fact, even earlier than that when we realized several years ago that we were down to just one licensed flu manufacturer in the United States. And I think people have worked very hard to get to the point that we are today, and now we need to the get to the point where we have much more domestic manufacturing capacity.

I think in the case of CSL, they are based in Australia and they have a similar kind of arrangement and requirement with the Australian government. You remember that the southern hemisphere has its outbreak at a different time, so Australia was experiencing a pretty severe outbreak and decided that it needed vaccine first for its home country.

Now, when that happened, CSL let us know that right away. We immediately were able to downgrade our projected numbers of doses of vaccines and at the same time we worked very closely with the manufacturer so that as soon as they met their requirement for their home country, they were able to start making and shipping doses to us.

In addition, I think as you heard, they have also submitted additional data recently so that their vaccine can be used down to a lower age in children. That was really recently licensed.

Ms. BALDWIN. I, also in my opening statement, talked a little bit about using this pandemic, this seasonal flu as well as the H1N1, to learn and to innovate, and I am wondering what your thoughts are in three particular areas. One is faster manufacturing processes, whether it is cell-based or other opportunities there; use of adjuvants; and alternative methods of vaccine delivery, something other than injection and nasal spray.

If we were to have a very virulent influenza next year, where would be in a year that we aren't today? What is your sort of time

horizon for when these innovations are going to be generally more available?

Dr. LURIE. I think that is really a great question. I think, again, BRTA is in, right now, year three of a five-year strategic plan to really try to move us toward more modern manufacturing technologies and manufacturing capacity in the United States.

As I said, the first cell-based facility has its ribbon cutting next week in North Carolina, but it actually I don't think it is going to be able to make flu vaccine for another year. But when all is said and done, that ought to get us to the point where they will be able to make I think 150 million doses. So that is still far short of the capacity, the surge capacity, we would need in a public health emergency.

In addition, cell-based vaccines still require the virus to grow in cells, so we need to move toward recombinant technologies and other kinds of technologies. We have invested in some of those. I think there is a lot of promise in a number of the new methodologies. I can't yet predict when they are going to come on line.

But I also want to say that it is great to be able to do those things, but once you do them, we can't forget that we have to manufacture to scale with whatever those are. So we have to be thinking now about, you know, how those new technologies and manufacturing capacity meet one another, so not everything is done one after another. So that is I think another real challenge that we have.

With regard to adjuvants, I think we all know and believe that adjuvants have a lot of promise. And just to reiterate, adjuvants really are used for two reasons. One is so you need less vaccine. The other is if you don't get a good immune response to that vaccine, they help you get a better immune response. It is a substance that you mix with the vaccine.

There is a lot of work going on right as we speak to understand the experience with adjuvants, trials being done by the manufacturers, as well as by NIH mixing one company's adjuvant with another company's vaccine to make sure those things are safe and effective. Depending on the outcome of those trials, I would expect that if they are promising, that the manufacturers will submit applications to the FDA. But we are not there yet.

Then in terms of the alternative methods, people are working on things like patches, a transdermal method. Some people are work on vaccines that you can eat. There is a lot of very exciting breakthroughs in the science that I think are going to move us far forward. Some are more ready than others. But it would be great if you could use a patch instead of a shot, for example.

Mr. BALDWIN. It is my understanding some of that technology also may have an impact on increasing the effectiveness of the vaccine. For example, skin micro-needle application versus injection.

Dr. LURIE. Right. And I think we are continuing to learn more about those. But I think a lot of these new technologies are very promising in terms of also being able to get a better immune response. It is really the immune response and it is sort of how it gets into the body to make that immune response that is the difference in some of these technologies.

I don't know, Dr. Goodman might want to amplify on that.

Dr. GOODMAN. I would want to add one thing, which is there is a lot of amazing innovation incredibly promising technologies.

We have licensed cell-based vaccines in this country, just not for influenza. That has been a real challenge. We have licensed recombinant vaccines in this country, just not yet for influenza. And I think those things are making some real technological progress, and those are things we are going to see progress in very soon.

But one thing I wanted to say is we see, even in the most sophisticated manufacturing technologies, there are still challenges producing large amounts of things consistently and of high quality. So even with some of the most advanced biotechnology products out there today, this is complex, challenging manufacturing, and it is not like just—I mean, the egg has been amazingly efficient and for some of the problems relatively reliable. Clearly it is an old technology. It has many disadvantages.

But I am just pointing out that some of the newer technologies are going to need the same kind of care, and that what works in a mouse or works in a very small production is not always the same and sometimes takes some time to get it to industrial scale and be sure it is going to be safe and high quality for people.

But we are all working together to accelerate that, because our goal should be for an emerging infectious disease threat, to have vaccines much, much faster, much, much faster, and there is promising technology that can help us do that.

Mr. PALLONE. Thank you.

I want to thank all of you for your comments today. I know that we did have some questions that I and others asked if you could get back to us in writing. The process is that members can submit additional questions in writing to you and usually they are supposed to be submitted within the next 10 days. So you may get some additional written questions to respond to as well.

But thank you very much really for such an important issue and that you are so involved in.

You had some comment?

Dr. LURIE. I wonder if it might be oK if I responded to something I heard in a couple of comments earlier.

Mr. PALLONE. Of course.

Dr. LURIE. I was very concerned and we haven't really had a chance to I think correct some misunderstandings here, and that has to do with vaccines going to Guantanamo or vaccines going to terrorists.

There is no vaccine on its way to Guantanamo. There is no plan to vaccinate terrorists or Khalid Sheikh Mohammed ahead of anybody else right now. That is a program that is handled by DOD. But I think it is one of those things that gets out there in a sound bite and it sort of travels virally and there is a lot of misinformation out there. There is no vaccine on its way there.

Mr. PALLONE. All right. Thank you very much.

Did you not—I am sorry, Mr. Gingrey is here. He hasn't had a chance to ask questions. So, go ahead. The gentleman from Georgia is recognized.

Dr. GINGREY. Mr. Chairman, thank you. I am pleased that the first panel is still here.

You know, I have some concerns. In the interest of full disclosure, I have been a bit of a doubting Thomas as a physician-member about our response to this crisis, this pandemic as it is now, and, of course, my great concern was us creating a pandemic of fear. I think we have certainly done that, and we also have since 2006 when we were dealing with avian flu probably in the aggregate have appropriated something like $12 billion or $13 billion. Feel free to correct me if I am wrong on my numbers, but a lot of money.

And, of course, as we track this and the concern was whether or not to develop and spend billions of dollars in the process and develop a vaccine specific to H1N1, different, of course, from the regular vaccine that we will be producing for seasonal flu. I think the decision was going to be made, I guess was made, on the basis of how virulent this strain became and what kind of changes might occur, was it getting worse. And I think you have said in your testimony, maybe all three of you, that the strain really hasn't gotten worse and the virulence has not increased.

But one thing that I did notice here lately was that all of a sudden we went from 1,000 deaths in the United States literally overnight to 4,000, and that is, I find, a little disingenuous. But there has been this explanation that, oh, well, we originally were basing cases of H1N1 on laboratory evidence, but now we are using a mathematical formula that we kind of extrapolate or estimate. Some people maybe in the CDC ought to go to work for the Census Bureau with those kind of calculations.

I have real concerns about that. In fact, I brought along with me a blank death certificate where it says "cause of death" and "contributing factors" and that sort of thing. I would be really curious to know how many of those 4,000 cases does the death certificate say the cause of death is H1N1 viral influenza.

Dr. SCHUCHAT. Thanks for those comments. Communication is really important to all of us and being clear and not confusing. We did not overnight go from 1,000 deaths to 4,000 deaths. All along we have been talking about using a variety of surveillance systems appropriate to the period of the pandemic and the efficiency of data collection, and we have said that reported cases underestimate the true burden of disease.

With seasonal influenza, when we talk about how many deaths or how many hospitalizations there are, that is not based on individual reporting by doctors and health departments and so forth. It is based on looking at a lot of different data sources and modeling those data.

What we did last week was release estimates that took information from a couple very good surveillance systems: Hospitalization data from our emerging infections program network in 10 different States; information from 30 or 35 States, depending on the week, about laboratory confirmed hospitalizations and laboratory confirmed deaths. We use those two as a ratio to understand from hospitalizations how many deaths might there be.

We looked at the influenza-like illness surveillance system, our sentinel providers, to divide up States into high, medium and low at any one time in terms of how common the transmission was. And then we used correction factors based on community surveys

done to really understand how many illnesses are in the community, based on household telephone surveys, for everyone who actually goes and sees a doctor, how many people that see a doctor get a lab test.

Dr. GINGREY. Dr. Schuchat, with all due respect, because my time is limited, I want to make one other point. I appreciate your explanation. I hope all of the panelists, all three doctors understand my concern.

The State University of West Georgia is in my district in Carrollton, Georgia, and they weren't having a problem getting access to the vaccine. I know that has been the main theme of this hearing, why we didn't develop, I don't know, millions, literally 50 million vaccines by a date certain in October, and it was only 15 million or whatever.

But the State University of West Georgia had no problem. They had plenty of vaccines. They have 11,500 students, and only 141 were willing to be vaccinated. A lot of them are very concerned. Let me give you a quick quote.

"Most students are saying that they haven't gotten the swine flu yet, so they believe that they are not going to get it at all," said Shandra Jones, a student, who is from Franklin, Georgia. There are also people telling students not to get the shot. There are some who are afraid of the side effects of the shot, and they've read about 1976 and Guillain-Barr Syndrome. They believe that the government did not test the shot enough."

Mr. Chairman, I know I have extended beyond my time. If the panel, if you would allow them as a courtesy to respond to this, because I think this is a huge issue. I don't care, if we have got 100 million vaccines and 10 percent of the population is willing to take the vaccine, even those that are high risk, what have we really accomplished here?

Mr. PALLONE. I am going to let you answer Mr. Gingrey's question, but also I have to be careful here, Dr. Lurie, because you opened it up to the Guantanamo thing. Chairman Stupak wants to say something too. So we will do those two and then be done—no, we are not done. Mr. Green is here. I give up.

All right, Mr. Gingrey. Respond to Mr. Gingrey.

Dr. SCHUCHAT. Sure. You raised one of the most challenging aspects of this pandemic. At the very same time people are waiting in line, driving hours to find vaccine, we have supply way in excess of demand in some communities. We have huge information needs to fill, and I think we are really committed to break the myths about the safety of this vaccine, what we do know and what we don't know.

There is a Web site, flu.gov, that has a lot of information about myths and facts that might help some of the college students understand what is the case. We have actually planned for some more outreach for youth, such as college students, to try to reach them and have them understand what is the threat to them, what are the risks or not about the vaccine.

But we have this very exquisitely challenging time where do we risk raising demand in some communities like that, at the same time we have so much extra demand versus our supply elsewhere. And that is one the reasons why we have really focused on State

and local support, because in your community, your public health experts understand on the ground, you know, we got a supply-demand mismatch the other way at West Georgia College, whereas in the national level, we may not really understand the community supply and demand.

So really one of our reasons to focus on State and local distribution or direction of where the vaccine goes is because of that trust of the community and that awareness of what is going on with your local community. So I think, if you want to get back to Gitmo—OK.

Mr. PALLONE. Are you done with Mr. Gingrey's response?

Mr. Green, let me just explain what happened is it looked like we were done and there was nobody here, so Dr. Lurie asked to take some time to talk about terrorists in Guantanamo, and Mr. Stupak just wanted to clarify and ask a question about that. Then we will go to you.

Mr. STUPAK. Dr. Lurie, you don't have anything to do with the military and getting the control of the drug to the military, do you?

Dr. LURIE. No, this whole program is run by the Department of Defense.

Mr. STUPAK. Right. Some you don't know if people at Guantanamo have received it. If anyone at Guantanamo has got it. You don't know if the 218 international terrorists we hold in U.S. jails has received it. You don't know that, because that is handled by a different party?

Dr. LURIE. Well, what I can tell you is like all militarily installations run by the Department of Defense, and they have pretty strict criteria, just like we prioritize vaccine going to U.S. Forces, deployed health care workers, civilians and contractors, civilians, et cetera.

Mr. STUPAK. The point is under oath you said they did not receive it. You don't know that. When Major Diana R. Haynie says they will be receiving it on November 2nd, they could already have the vaccines down in Guantanamo. This was November 2nd and it is now, what, the 18th. Sixteen days ago. They could have it there. You don't really have any personal knowledge of it?

Dr. LURIE. No, I am sorry. What I was trying to do was correct a misconception about how the vaccine was distributed. I do not have personal knowledge of that.

Mr. STUPAK. Correct. I realize uniformed personal first are required to do it, and even these detainees will have a right to accept it or refuse it. But the point being, this was released at November 2nd at the time of the height of the shortages, and the American people are upset about it.

I have no problem. I just say you are under oath. Don't be testifying to things you don't have any personal knowledge of.

Dr. LURIE. Fair enough.

Mr. PALLONE. All right. Mr. Green.

Mr. GREEN. Thank you, Mr. Chairman. I appreciate the patience of our witnesses. You have been here a long time, plus you had to listen to our opening statement. But that is just the way it works here some times.

I appreciate your being here. I guess the frustration is because we have had, both the Health Subcommittee and I benefit, I am on both the Health Subcommittee and the Oversight, and we have had

a number of hearings since the spring, and the most recent one in September, and it seems like the best plans that we had just didn't pan out. And it is not necessarily with the delivery system. We will hear from that at the next panel. We have the Commissioner, but we will also have on the manufacturing side the next panel.

But there has been talk for many years about what we need to do for pandemics, and yet here we have what relatively can be major. A month ago we had a Homeland Security hearing in Houston, Texas, and we had 1,000 people died. Now it is up to 4,000. If it had been something much worse than H1N1, we would be sitting here and saying why are we having tens of thousands of people dying from avian flu?

What do we need to do, or the agencies, all your agencies and even Congress, need to do to live up to the plans and expectations that we had from the earlier hearings where we were going to have enough vaccine, the distribution system was there. Right now we don't know if the distribution system is there simply because we don't have enough vaccines, all we know something is working because people are lining up all over the country to receive it.

The other question I have is my concern that the lack of regular flu vaccine, or at least the participation, and the one thing we know now is hopefully next year or the next flu season we will have H1N1 in with the seasonal flu, but that we need to make a national effort to increase the seasonal flu vaccinations. That comes from all of us. We have seen a little up-tick because of the fear of H1N1, but I want to see what we can do to—the cheapest thing we can do for the business community is a flu shot for their employees.

So with that, and the time I have, 2½ minutes for all three of you.

Dr. SCHUCHAT. I think there are several things we could do to strengthen our response for seasonal flu as well as for a future pandemic, which I do believe we will have. We have a public health infrastructure that is weak right now. It has suffered many job losses, many furloughs, and it leaves us a little bit of a weakened core to respond to this kind of thing.

We do not sufficiently use information technology that could help connect the electronic health records in the private health care system with public health needs. We could do much better targeting of priority groups if we had better information systems. Some States have immunization registries that work pretty well, but they don't often reach to adults. We don't have a strong adult immunization program in the U.S. Adult providers haven't yet really stepped up the way pediatricians have to use prevention at the forefront.

Mr. GREEN. I appreciate that, and we are going to run out of time, but we are talking about pediatricians, and we have a really robust vaccination system for children. We know H1N1 targets children and young adults. I had my 62nd birthday three weeks ago, and for the first time I said I am glad I am 62, because H1N1 doesn't hit us that much. But we have that system now. The problem is we don't have the vaccinations.

Dr. SCHUCHAT. Right. I think there is two things though. We certainly need a more robust vaccine production with the new technology, broader manufacturing capacity. But with children, if you

look at this pandemic, it is really disproportionately affecting school age children, and they don't go to the pediatricians very often and they don't get vaccinated very often compared to younger children, 1-year-olds and 2-year-olds. So there is a tremendous opportunity to strengthen immunization for school age children.

Many States are having great experiences with school-located vaccinations for H1N1. Those could be models for seasonal flu, for instance, in the future. But there is a lot of work to do before we would realize the very efficient delivery system that we would like to have.

Dr. LURIE. Certainly. And I would really second Dr. Schuchat's comments about really strengthening the public health infrastructure at all levels. In addition, as we have talked about some already this morning, we do need to get to much more robust manufacturing technologies.

We talked about the fact that there are some promising new developments, and we need to continue to invest in pulling those kinds of technologies along so that they can make vaccines faster and more reliably. And then those new developments have to somehow meet the large scale safe manufacturing capacity so that were we to have another emerging infectious disease, another kind of pandemic, that would be able to get vaccine out in very large quantities much faster and not be reliant on the vagaries that we have now.

Mr. GREEN. Mr. Chairman, I know I have run out of time, but those of us who are from the sugar cube generation that dealt with polio, I know we use that example many times in our hearings, I think our agencies need to look at that and say how do we deal with this. Because next time it won't just make us sick for a few days, it may be killing a lot more people than just 4,000, because we lose 36,000 people every year from regular seasonal flu. But I am worried about the pandemic on something much more serious.

Thank you, Mr. Chairman.

Mr. PALLONE. Thank you.

I guess I am going to say thank you again. I won't repeat what I said again though. Thank you so much, and again get back to us with any written comments. We would appreciate it.

Now we will call the second panel.

Mr. STUPAK. [presiding.] We will call our second panel up. This panel includes Mr. Paul Perreault, the President of CSL Biotherapies, Incorporated; Dr. Vas Narasimham, President of Novartis Vaccines USA; Dr. Ben Machielse is Executive Vice President of operations for MedImmune; Dr. Phillip Hosbach is Vice President of Immunization Policy and Government Relations for Sanofi Pasteur; Dr. Lakey is Commissioner of the Texas Department of State Health Services; and Dr. Jeffrey Levi is Executive Director of Trust For America's Health.

TESTIMONIES OF PAUL PERREAULT, PRESIDENT, CSL BIOTHERAPIES, INCORPORATED; DR. VAS NARASIMHAM, PRESIDENT, NOVARTIS VACCINES USA; BEN MACHIELSE, EXECUTIVE VICE PRESIDENT OF OPERATIONS, MEDIMMUNE; PHILLIP HOSBACH, VICE PRESIDENT, IMMUNIZATION POLICY AND GOVERNMENT RELATIONS, SANOFI PASTEUR; DR. DAVID LAKEY, COMMISSIONER, TEXAS DEPARTMENT OF STATE HEALTH SERVICES; AND DR. JEFFREY LEVI, EXECUTIVE DIRECTOR OF TRUST FOR AMERICA'S HEALTH

Mr. STUPAK. I welcome all of our witnesses to testify here today. In accordance with the policy of the Oversight and Investigations Subcommittee, witness testimony will be taken under oath. Please be advised that under the rules of the House, you have the right to be advised by counsel during your testimony.

Do any of you wish to be represented by counsel?

Everyone is shaking their head no, so I will take that as a no. Therefore I am going to ask you to please rise and raise your right hand to take the oath.

[Witnesses sworn].

Mr. STUPAK. Let the record reflect the witnesses have replied in the affirmative. You are now under oath.

We will now hear a 5-minute opening statement from each of our witnesses. You may submit a longer statement for inclusion in the hearing record.

Mr. Perreault, we will start with you, for 5 minutes, please, sir, your opening statement.

TESTIMONY OF PAUL PERREAULT

Mr. PERREAULT. Thank you, and good afternoon, Chairman Stupak and Chairman Pallone and members of the committee. I am Paul Perreault, President of CSL Biotherapies, Incorporated, the U.S. distributor of influenza vaccines manufactured by our parent company CSL Limited, located in Melbourne, Australia.

I am pleased to be here today to discuss our experience in manufacturing the H1N1 vaccine specifically for the United States. CSL Biotherapies believes that it is important to understand how the government and industry can best work together to help assure vaccine availability for influenza pandemics.

I want to assure this committee that CSL Biotherapies is committed to providing the entire amount of both the H1N1 bulk antigen and the finished vaccine doses that we have agreed to in our contract with the Department of Health and Human Services. We take the H1N1 pandemic very seriously and have been a leader in developing and delivering to combat this virus.

CSL has manufactured vaccine since its founding in 1916. Our world class influenza vaccine production facilities have the capacity to produce up to 80 million doses of trivalent seasonal influenza vaccine annually. Our seasonal flu vaccine Afluria was launched in the United States in October 2007 and indicated for ages 18 and above. And as you heard Dr. Goodman state, last week Afluria and our H1N1 vaccines received FDA approval for administration to individuals 6 months through 17 years of age as well. Afluria and our

H1N1 vaccine come in multi-dose vials and thimerosal-free prefilled syringes.

CSL initiated the western world's first human trials with the 2009 H1N1 vaccine and published our research findings in the New England Journal of Medicine demonstrating the efficacy of a single 15 microgram dose. These data, along with the rules of clinical trials in infants and children, were communicated rapidly to regulatory and public health authorities in the United States and globally, recognizing their value to public health decisionmaking.

In May 2009, HHS and BARDA approached CSL Biotherapies to inquire whether we might be able to provide an H1N1 vaccine for the United States. CSL Biotherapies entered into a one-year special contract initiated on May 28th, 2009, to provide 36 million dose equivalents of H1N1 bulk antigen to the United States Government. CSL Biotherapies did not have a previous pandemic contract with the United States Government.

As part of the agreement signed in May, CSL Biotherapies made it clear that the company had a preexisting contractual obligation with the Australian government to provide vaccine to that nation first, should WHO declare a pandemic. I want to stress this had no impact on fulfilling our schedule submitted to BARDA.

On June 1, 2009, CSL received the first H1N1 virus vaccine seed from the New York Medical College. The yields from this lot were approximately one-third to one-half of the average H1N1 seasonal influenza yield. As a result of these low yields, CSL formally communicated to BARDA a delay to the overall timing of the H1N1 bulk antigen delivery.

On the 18th of August, CSL received a new vaccine virus seed that was introduced into the manufacturing process. Yield improvements in excess of 80 percent compared to the previous seed were observed. A revised supply schedule was sent to HHS on September 14th incorporating production on this seed lot.

CSL remains committed to maximizing the yield and availability of H1N1 vaccine. CSL has invested in fill-and-finish capabilities in Europe and Kankakee, Illinois, to improve the availability of influenza vaccine. The Kankakee facility has achieved licensing of its new state-of-the-art syringe fill-and-finish line this past September.

I would like to recommend measures to help assure availability of pandemic vaccine. First I would recommend there be a focus on producing a greater assortment of influenza seed lots earlier that can be utilized in the creation of future pandemic influenza vaccines. The poor yields resulting from the first available seed lot had a significant effect on reducing the amount of available H1N1 vaccine. If the 10-week gap in identifying the second higher yielding seed lot could have been avoided, higher output could have occurred sooner.

Second, new adjuvants can help to enhance the immune response and reduce required dosing, which would make more antigen available for additional vaccinations. Supportive environment for development of new adjuvants with influenza vaccine could facilitate in this advancement.

Finally, more education about the benefit of influenza vaccination and the achievement of higher vaccination rates closer to CDC

recommendations would help to prevent influenza and support readiness.

Our passion at CSL Biotherapies is to help save and improve lives, and we wish to do our part in protecting the United States population from H1N1 and seasonable influenza. We'll continue to work with the government collaboratively.

Thank you for the opportunity to speak before the committee, and I welcome the opportunity to answer any questions.

[The prepared statement of Mr. Perreault follows:]

Statement of Paul Perreault
President, CSL Biotherapies, Inc.
Before
The Energy and Commerce Subcommittee on Oversight and Investigations and the Subcommittee on Health
Concerning
H1N1 Influenza Vaccine Preparedness

November 18, 2009

Good morning Mr. Chairman and members of the committee. I am Paul Perreault, President of CSL Biotherapies Inc., the U.S. distributor of influenza vaccines manufactured by our parent company CSL Limited, located in Melbourne, Australia. I am pleased to be here today to discuss our experience in manufacturing the H1N1 vaccine specifically for the United States. We believe it is important to understand how the government and industry can best work to help assure vaccines for influenza pandemics.

I want to assure this committee that CSL Biotherapies, Inc. is committed to providing the entire amount of both the H1N1 bulk antigen and the finished vaccine doses that we have committed to in our contract with the Department of Health and Human Services (HHS). We take the H1N1 pandemic very seriously and have been a leader in developing and delivering a vaccine against it.

About CSL Limited

CSL is a leading global biopharmaceutical company with headquarters in Melbourne, Australia. The company researches and manufactures vaccines and therapies for rare and serious conditions. CSL originated in 1916 when it was formed to provide vaccines and therapies to the Australian population. It now has a presence in 27 countries with worldwide research and manufacturing. The company has a major manufacturing facility in Kankakee, Illinois and its headquarters in King of Prussia, Pennsylvania for CSL Biotherapies, Inc. and CSL Behring, CSL's global plasma therapies division for rare conditions such as hemophilia, primary immune deficiency and genetic emphysema.

CSL Seasonal Flu Vaccine Production for the United States

CSL has manufactured vaccines since its beginning. As CSL grew, we were able to provide influenza vaccines in more countries; first in the southern hemisphere and more recently in the northern hemisphere. Our world class influenza vaccine production facilities have the capacity to produce up to 80 million doses of trivalent seasonal influenza vaccine annually.

Our seasonal flu vaccine, Afluria™ was launched in the United States in October 2007. Afluria™ was first indicated for ages 18 and above in the United States. I am very

pleased to report that Afluria™ received approval on November 10, 2009 for administration to individuals six months through 17 years of age. The same indication was provided simultaneously for our H1N1 vaccine.

Afluria™ is manufactured at our facility in Melbourne, Australia. However, fill and finish of our vaccine for the United States – where we finish the vaccine doses and "fill" them into pre-filled single dose syringes or multi-dose vials - is being performed in a newly licensed, state of the art syringe filling line in Kankakee, Illinois and a modern facility in Marburg, Germany. Pre-filled syringes of Afluria come in a thimerosal-free formulation.

In late September 2009, CSL Biotherapies entered into an agreement to license sole distribution rights of Afluria™ to Merck in the United States, which further assures the distribution of this valuable vaccine in this country.

CSL Production of H1N1 Vaccine for the United States

CSL is committed to providing H1N1 vaccine. CSL initiated the western world's first human trials with a 2009 H1N1 vaccine, and published research findings in the *New England Journal of Medicine (*Greenberg ME et al, NEJM 2009; 361), that had a major impact informing vaccine policy globally. The interim findings of this trial were the first to establish that a single 15 microgram dose of the unadjuvanted vaccine was well-tolerated and highly immunogenic in adults. This helped establish the policy that only one dose of the vaccine would be needed instead of two doses as had been presumed. These data, along with results of clinical trials in infants and children were communicated rapidly to regulatory and public health authorities in the United States and globally, recognizing their value to public health decision-making.

In May 2009, the Office of the Biomedical Advanced Research and Development Authority (BARDA) approached CSL Biotherapies to inquire about whether we might be able to provide an H1N1 vaccine for the United States. CSL Biotherapies worked with BARDA and entered into a one-year special contract, initiated on May 28, 2009 to provide 36 million dose equivalents of H1N1 bulk antigen to the United States government for the 2009-10 flu season (CSL did not have a previous pandemic contract with the United States government). As part of this agreement, CSL made it clear that we had a pre-existing contractual obligation with the Australian government to provide vaccine to Australia first, should the World Health Organization declare a pandemic, which it did. I must stress that CSL Biotherapies' commitment to Australia in no way impacted our schedule to provide vaccine to the United States.

Our initial estimates for 2009 H1N1 vaccine production capacity were based on several factors: expected yields for the novel H1N1 flu strain based on our prior experience producing H1N1 influenza virus strains; timing, logistics and plans to shift our manufacturing from seasonal influenza vaccine for the Northern Hemisphere to novel H1N1 vaccine production as a monovalent vaccine. We carefully analyzed our capacity based on expected yields and the ability to process 300,000 eggs per day.

Delivery of H1N1 bulk antigen was impacted versus original estimates due to lower yield for this novel strain of H1N1 versus previous H1N1 seasonal influenza strains. It must be understood that the production of influenza vaccine is a biological system and as such the speed of availability of vaccine doses is often more related to the ability of the virus to be grown in the chosen substrate (whether eggs or cells) than any other constraint. It is not always possible to ensure the virus will grow well.

Difficulties with the H1N1 Vaccine Seed

On June 1, 2009, CSL received the first H1N1 virus vaccine seed from the New York Medical College. CSL began developing a seed lot and bulk manufacturing activities on June 19. CSL observed lower than expected yields. The yields were approximately one third to one half of an average H1N1 seasonal influenza yield. As a result of these low yields a revised delivery schedule was created and sent to HHS on July 2, 2009.

CSL promptly initiated a program to investigate improvements to yields including egg incubation temperatures and inoculation concentrations. CSL made a number of incremental improvements to the manufacturing process, resulting in a yield improvement of 10% over that obtained using the initial virus vaccine seed lot.

On August 18, 2009, CSL received a new vaccine virus seed from the New York Medical College that was introduced into the manufacturing process on September 4, 2009. Yield improvements in excess of 80% compared to the previous seed were observed in the initial lots using indicative in-process measurements. Manufacturing of H1N1 bulk antigen is in progress according to a revised supply plan sent to HHS on September 14, 2009. On October 30, 2009, CSL provided the latest delivery schedule to HHS with an increase in the finished dose output volumes.

CSL remains committed to maximizing the yield and availability of the H1N1 virus vaccine. To this end, improvement projects, such as optimizing incubation conditions and inoculation concentrations, are continuing within the manufacturing area. CSL also invested in fill and finish facilities in both Europe and the U.S. to improve availability of seasonal and pandemic influenza vaccine and achieved licensing of our U.S. facility for fill and finish this year, working closely with FDA.

I would like to take this opportunity to highlight the cooperation that CSL Biotherapies, has experienced with BARDA. This agency has worked collaboratively to put in place the original contract and has stayed in close touch throughout the seed lot and production schedule changes. I am in frequent contact with the BARDA staff. BARDA's and HHS' focus and sense of urgency in bringing H1N1 to the United States aided CSL's ability to deliver H1N1 vaccine to the United States.

Cell Based Versus Egg Based Vaccine Technology

Because egg-based technology has been in existence for some time, there are some misconceptions that egg-based vaccine technology is outdated and somehow might be responsible for slower production of H1N1 vaccine. CSL uses and continues to believe in egg-based technology. We use this technology for both our seasonal flu vaccine and for the H1N1 vaccine. There is nothing different about the H1N1 vaccine manufacturing process compared to that of regular seasonal flu vaccine, except for the virus strain.

In the past 3 to 4 years, CSL Biotherapies, Inc. and other major manufacturers have invested heavily in expanding egg based production capacity. All seasonal influenza vaccine used in the U.S. and the vast majority of that used in the rest of the world, is derived from egg based manufacturing.

The misconceptions surrounding egg versus cell technology include the following:

i) Production is limited by availability of eggs
In Australia, at CSL, manufacturing occurs for both northern and southern hemispheres. Eggs are available all year round and have not constrained our production.

ii) Time is lost in developing suitable seed virus for manufacture in eggs
It is true that some time is required to achieve good production yields with many strains regardless of the medium. However, the record to date shows good production can be achieved in eggs far more reliably for difficult strains than in cell-based technology.

iii) Length of process is longer in eggs
Processing time is similar for eggs and cells.

iv) Cells can produce more efficacious vaccines
The performance of both CSL's vaccine and manufacturing system were clearly demonstrated in the recent H1N1 clinical trials conducted both in the U.S. and Australia. These trials, as referenced in the New England Journal of Medicine, illustrate the positive impact our H1N1 flu vaccine will have in protecting the population from the virus. These clinical trials were conducted with vaccine doses manufactured from egg based technology.

CSL has been conducting a development program in cell culture influenza vaccine manufacturing for a number of years. We have evaluated many different cell lines, and in our opinion, all have been shown to be unreliable in either performance at large scale or in yield of virus. None were as reliable as eggs in producing good yields for all strains.

More recently, CSL has evaluated a new cell line that we believe shows the most promise for reliable production. We are currently evaluating our options for this approach.

CSL believes it will be many years before cell culture is advanced and efficacious enough to challenge egg technology as the preferred means of production, even as we have engaged in exploring the possibility of cell-based production. We also believe that the technology currently used is well suited to ensuring the most rapid response to meeting U.S. requirements at this time.

Recommendations for Improvements in the System

Seed lots - I would recommend there be a focus on producing a greater assortment of influenza seed lots earlier that can be utilized in the creation of future pandemic influenza vaccines. As we have seen, the poor yields resulting from the first available seed lot had a significant effect on reducing the amount of available H1N1 vaccine. If, for instance, the 10-week gap in identifying the second, higher yield seed lots could have been avoided, manufacturing could have occurred sooner. This would be my first priority, and in my view supersedes any concerns about cell based versus egg based technologies.

New adjuvants - could help to enhance the immune response and reduce required dosing, which would make more antigen available for additional vaccinations. A supportive environment for development of new adjuvants with influenza vaccine could facilitate this advancement.

Increasing vaccination rates - more education programs about the benefits of influenza vaccination, to help address fear or apathy, and vaccination rate increases to come closer to CDC recommendations for whom should be vaccinated, would help to prevent influenza and support readiness.

Conclusions

Thank you again for the opportunity to speak before the committee and answer questions. I hope today's hearing provides more insight into the complex world of H1N1 vaccine production. CSL and CSL Biotherapies, Inc. are committed to working with the United States government to produce and provide H1N1 flu vaccine as quickly as possible. Our passion at CSL and CSL Biotherapies, Inc. is to help save and improve patient lives and we wish to do our part in protecting the US population and other parts of the world from H1N1 and seasonal influenza. We will continue to focus on this goal and work with government collaboratively to accomplish that.

Mr. STUPAK. Thank you.

Doctor, would you like to testify? Pull that up and turn that mic on please.

TESTIMONY OF VAS NARASIMHAM

Dr. NARASIMHAM. Good afternoon.

I want to thank Chairman Stupak, Chairman Pallone, Ranking Member Walden, and the distinguished members of the committee for the opportunity to speak with you today.

Novartis Vaccines and Diagnostics is a leading global vaccine manufacturer headquartered in Cambridge, Massachusetts. Along with our predecessor companies, we have been a leader in the development and supply of influenza vaccines to the United States for over 25 years.

Today, I would like to highlight to the committee Novartis Vaccines' commitment to U.S. influenza pandemic preparedness in our dedication to prevent every possible illness and death from influenza. We commend HHS for its global leadership in pandemic preparedness over the last 5 years. We have had a broad and successful partnership with HHS, including active collaborations on cell culture vaccines, adjuvants, stockpiles and new production facilities.

Novartis Vaccines has committed approximately $1 billion in influenza vaccine development and production since 2006. Importantly, with HHS support we are constructing the first flu cell culture manufacturing facility in the United States located in Holly Springs, North Carolina, with its ribbon cutting later this month. This facility will help ensure the rapid availability of pandemic vaccine for the American people in the future.

For this pandemic, we have continued our commitment to U.S. pandemic response and public health. First, in May, we voluntarily dedicated the entire vaccine output from our manufacturing facility in Liverpool, England, to the United States. This facility represents over half of our global egg-based manufacturing capacity. We did this because of our long partnership with HHS, foregoing the potential opportunity to quadruple the output of this facility using our MF59 adjuvant.

Second, our entire organization has worked around the clock to support U.S. vaccine production. We've made large new investments, added 300 additional staff, accelerated new production lines, and have been operating our production facility with a high level of quality and efficiency.

Third, we rapidly started and enrolled a broad range of clinical trials in more than 9,000 children and adults in less than 3 months. Our data showed in early September a single dose, as opposed to two, is adequate for adolescents and adults; and we recently showed that a half dose might be sufficient.

Fourth, we have prepared for HHS to use our MF59 adjuvant that is currently licensed and being used exclusively in our products outside the U.S. for H1N1. We have demonstrated in recent U.S. Pivotal clinical trials that our adjuvant could significantly increase U.S. H1N1 vaccine supply.

Fifth, we successfully supplied 27 million doses of seasonable flu vaccine to the U.S. by early October.

Now, most importantly, in partnership with the U.S. Government, we have overcome tremendous challenges to produce a safe and effective pandemic vaccine in less than 3 months. These challenges have included low yields, multiple production uncertainties and compressed timelines. Despite these challenges, as of today, Novartis Vaccines has shipped over 18 million unadjuvanted doses to the U.S. Government; and we are fully on track with our production, a tremendous joint accomplishment.

We also believe, based on the experience this year, there are important opportunities to improve pandemic preparedness in the future. These opportunities include the need to move manufacturing into the 21st century for influenza vaccines using new technology such as our cell-culture-based technology now being used—licensed for seasonable pandemic use in Europe.

There is a need to accelerate regulatory pathways for novel influenza adjuvants and pandemic vaccines. We need to develop new testing methodologies to speed up vaccine formulation and quality release, which can often slow down vaccine availability. We need to maintain the strategic national stockpile for rapid deployment in the case of a severe pandemic. And, finally, as noted by other members, we must support seasonable influenza vaccination demand to ensure that suppliers are not forced out of the market, as has happened in the past.

Novartis Vaccines continues to do everything possible to maximize the rapid supply of a safe and effective vaccine in close collaboration with HHS. We believe that when taken into full context the productive public-private partnership to produce, test, and deliver a safe and effective H1N1 vaccine to the U.S. has been a remarkable success. We are fully committed together with HHS now and in the future to ensure we achieve our shared goal of preventing every influenza case in the United States.

Thank you. I welcome your questions.

[The prepared statement of Dr. Narasimham follows:]

NOVARTIS

Written Testimony Submitted to
Congress of the United States
House of Representatives
Committee on Energy and Commerce
Subcommittee on Health and
Subcommittee on Oversight and Investigations

Joint Hearing Regarding Vaccine Availability, Production and Distribution

November 18, 2009

Submitted by:

Vas Narasimhan MD, MPP
President, Novartis Vaccines, USA
Head of Novartis Vaccines North America

on behalf of

NOVARTIS VACCINES AND DIAGNOSTICS, INC.

Mr. Chairman, Members of the Committee, thank you for the opportunity to participate in today's joint hearing to examine the current state of H1N1 vaccine availability and the next steps in production and distribution efforts. I am Dr. Vas Narasimhan, President of Novartis Vaccines USA, and Head of Novartis Vaccines North America.

Novartis Vaccines welcomes the opportunity to provide perspective on our efforts to address the public health challenges posed by H1N1, our scientific contributions to vaccine development and pandemic preparedness and our long-standing partnership with the U.S. Government to help protect the public health of the United States. From the outset of this year's pandemic we and the U.S. Government have worked together toward the common goal of producing as many safe and effective vaccine doses as soon as possible, despite the challenge of a rapidly evolving and uncertain situation. We appreciate the impact that this pandemic is having on our population, including children, pregnant women, and high risk groups throughout the country. To address the public health challenges of H1N1, we have dedicated a large portion of our organization's resources since May to supporting the global response.

Novartis Vaccines continues to do everything possible to maximize supply of safe and effective vaccine as soon as possible based on the direction of the U.S. Government. I am pleased to report to you that Novartis Vaccines is currently on track with our H1N1 supply to the United States, despite the many challenges we have encountered along the way. We understand that the American people expected more vaccine earlier. However, we believe that when taken into full context this historic public-private partnership to produce, test, and deliver a safe and effective H1N1 vaccine to the U.S. has been a remarkable success given all the challenges and compressed timelines we have faced. Novartis Vaccines is committed to working together with HHS to ensure today and in the future we achieve our shared goal of preventing every possible case of influenza in the United States.

I would like to begin today by providing some background on Novartis Vaccines and our pandemic preparedness efforts. I will focus my remarks on our efforts to support the U.S. Government's pandemic response and potential areas for future investment and improvement.

I. Overview of Novartis Vaccines

Novartis Vaccines and Diagnostics was created in 2006 through the acquisition of Chiron Corporation. We have over 5,300 employees globally, including almost 1,300 in the United States. Since 2006, Novartis Vaccines has invested and committed over $1 billion to upgrade our vaccines business infrastructure and for pandemic vaccine research and development. Our global headquarters is located in Cambridge Massachusetts, where Novartis Vaccines has a significant administration presence and a newly established research center dedicated to advancing innovative vaccines research in virology. The company also has a significant presence in Emeryville, California, the site of our global Diagnostics headquarters. In addition to our U.S. sites, we have manufacturing, research and clinical sites in England, Germany, Netherlands, Italy and India. Construction of our U.S.-based flu cell culture manufacturing site, the first of its kind in the U.S., was initiated in 2007 in Holly Springs, North Carolina and is currently nearing completion. By the end of November, this site will employ approximately 200

people and once fully-operational, it will employ approximately 350-400 people. A recent photo of this facility is attached as an Annex to this Testimony.

Novartis Vaccines is dedicated to preventing disease and addressing global public health needs. The company has a broad portfolio of approved vaccines globally and seventy percent of the vaccines we manufacture are supplied to the developing world. Novartis Vaccines continues to work towards introducing new important vaccine products to address unmet needs, with 17 new vaccines currently under development.

II. Novartis Influenza Vaccines and Pandemic Preparedness

Overview of Influenza Market

Since the circulating influenza strains change from year to year, influenza vaccine is the only FDA-approved drug or vaccine which is made anew from start to finish every year. Manufacturers commence vaccine manufacturing at risk prior to the Food and Drug Administration's (FDA) selection of the virus strains, in February, for the following fall's immunization season. Manufacturers receive the seed strains from the regulatory authorities so that there is consistency across manufacturers of the product provided to the market. From February-September each year, manufacturers manage the complex biological manufacturing process and work closely with regulatory authorities to successfully bring influenza vaccines through clinical development, manufacturing and regulatory approval.

Over the past three years, seasonal influenza vaccine manufacturers have faced an oversupplied and challenging marketplace. Immunization rates of the American public only rose 1% from 2007 to what is anticipated in 2009, from approximately 107 million to 110 million vaccinations. This immunization rate falls far short of the U.S. Public Health Service recommended level of 220 million Americans. As a result, the market has been oversupplied and prices have dropped by 30-40% creating a strong disincentive for manufacturers to maximize or even maintain current production capacity for the U.S. market.

Novartis Influenza Vaccines

Novartis Vaccines and its predecessor companies have been manufacturing influenza vaccines for the U.S. and the rest of the world for over 25 years. We are a leading innovator in the development of improved influenza vaccines through new technologies and novel adjuvants. Globally Novartis Vaccines has five approved seasonal vaccines, including adjuvanted and cell culture vaccines in Europe. We also have three approved H1N1 vaccines, including adjuvanted egg and cell culture based vaccines in Europe. We have over five large ongoing influenza development programs for the U.S. market.

Despite the trends in seasonal vaccine supply and demand, since 2006 Novartis Vaccines has established or improved our influenza manufacturing sites, in large part to address the challenge of global pandemic preparation. There are two investments that address U.S. influenza vaccines: our $200 million recently approved Site 4 bulk manufacturing facility in Liverpool, England and

our investment in our flu cell culture ("FCC") facility being constructed in Holly Springs, North Carolina with the support of HHS.

Proprietary MF59 Adjuvant

Novartis Vaccines has pioneered the study and use of influenza adjuvants over the past decade. MF59 is Novartis Vaccines' proprietary and patented adjuvant that is added to influenza vaccines to help stimulate the human body's immune response. In over 10 years of licensed use in Europe and experience in over 200,000 clinical trial subjects Novartis Vaccines has demonstrated the following benefits of adjuvantation:

- **Immunogenicity.** Adjuvanted vaccines produce higher immune response than unadjuvanted vaccines particularly in the elderly and young children;
- **Antigen Sparing.** Adjuvanted vaccines require a lower dose of antigen and have demonstrated the potential for a 2-4 fold expansion of vaccine supplies;
- **Cross-Protection.** Influenza viruses are constantly changing. Adjuvanted vaccines have show a higher likelihood of protecting against "drifted" and "heterotypic" changes in influenza strains;
- **Safety.** The safety of adjuvanted vaccines is comparable to unadjuvanted vaccines; and
- **Cross-Priming.** Adjuvanted vaccines have been shown to more broadly prime patients immune response (up to 7 years later) requiring fewer vaccinations to the newly circulating strain.

Outside of the U.S., in addition to adjuvanted seasonal flu vaccine, Novartis Vaccines is exclusively providing adjuvanted H1N1 vaccine. Our clinical data to date indicates that a single dose of adjuvanted vaccine with as low as 3.75ug of antigen meets the relevant regulatory criteria, compared to the 15ug dosage that we have manufactured for the American public to comply with regulatory requirements. We have been in discussions with the FDA since 2007 to license our MF59 adjuvanted prepandemic vaccine in the U.S. and in 2008 filed a Biologics Master File on MF59 to support this effort. However, currently no adjuvanted influenza vaccine is licensed in the U.S.

Cell Culture Vaccines

Novartis Vaccines has been a leader in developing and manufacturing influenza vaccine in cell cultures, and our flu cell culture product Optaflu was approved for use in Europe in 2007. Pioneered by Novartis Vaccines, flu cell culture manufacturing represents the first innovation in inactivated influenza vaccine production in over 50 years. It offers flexibility in the manufacturing process as the vaccine product is incubated using the tools of biotechnology rather than eggs. Cell culture-based vaccines provide three principle benefits: faster production, better matched vaccines, and no reliance on eggs. Our adjuvanted cell culture H1N1 vaccine was first produced in early June of this year, met all relevant regulatory criteria after extensive

clinical testing, and has been approved for use in Germany with other country approvals expected shortly.

We are presently working in partnership with the U.S. Government as part of its pandemic preparedness effort to develop this technology for the United States. Novartis Vaccines submitted a BLA to FDA for our cell based influenza vaccine in February 2009 and this submission contained all the required data for pivotal trials required by FDA guidelines. We withdrew the BLA at the request of FDA to incorporate data from an efficacy trial that agency officials were aware had been recently completed. Novartis Vaccines plans to resubmit this BLA once this data and data from other recently completed studies have been incorporated into the BLA. Prior to the 2009 H1N1 pandemic, Novartis Vaccines had prioritized this but we interrupted our efforts to dedicate critical personnel to H1N1 activities and, for this reason, we plan to re-focus on this BLA once these employees' H1N1 responsibilities permit.

III. HHS-Novartis Vaccines Pandemic Vaccine Partnership

Novartis Vaccines has been at the forefront of pandemic vaccine research, developing one of the first vaccines for H5N1 (commonly called avian flu) shortly after the strain was identified in 1997. For the past 8-9 years, pandemic preparedness has become a public health priority and the U.S. Government has provided global leadership in this effort.

In 2005, the United States Congress and the Administration took an unprecedented step to protect public health through the pandemic preparedness program which is now firmly established under the Biomedical Advanced Research and Development Authority (BARDA) located within the Department of Health and Human Services (HHS). Since 2005, Novartis Vaccines has established an extensive and highly productive collaboration with BARDA on pandemic preparedness, and we place the highest possible priority on working in partnership with the U.S. Government to address the United States' public health challenges.

Through this partnership, Novartis Vaccines is collaborating with HHS-BARDA on four major efforts: clinical development of flu cell culture technology, clinical development of antigen sparing (adjuvant) technology, production for pre-pandemic stockpile supply, and design, construction and operation of a flu cell culture production facility in the United States.

In January 2009, more than two years after beginning construction at our own expense, Novartis Vaccines was awarded a cost sharing contract for the construction of our U.S. flu cell culture facility in Holly Springs, North Carolina. At present, construction at the Holly Springs facility is near completion and Novartis Vaccines expects that the bulk facility will be licensed to provide cell culture-based vaccine for the 2013-2014 flu season. When fully operational, this facility will have the capacity to produce up to 50 million doses of seasonal flu vaccine and up to 150 million doses of adjuvanted pandemic vaccine for the United States within 6 months of the declaration of a pandemic.

IV. Novartis Vaccines 2009 US H1N1 Pandemic Response

With the above history as context, I would like to now turn to our current effort to respond to the 2009 H1N1 pandemic. As noted, over our 4 year partnership with the U.S. Government, Novartis Vaccines has worked closely with HHS on all aspects pandemic preparedness. As stated earlier, from the outset of this pandemic we have shared the common goal of producing as many safe and effective vaccine doses as soon as possible.

Novartis Investments in Vaccine Development and Production

This year, Novartis Vaccines undertook an unprecedented manufacturing effort to meet extraordinary demands created by the need for both seasonal and H1N1 pandemic vaccine in the United States. Novartis Vaccines has undertaken a number of these steps "at risk" to ensure no loss of time in development or supply. Novartis Vaccines is proud of what it has accomplished in responding to the challenges of the H1N1 pandemic. Some of these accomplishments are highlighted below:

- **U.S. H1N1 Clinical Development.** Novartis Vaccines developed both pilot and pivotal clinical trials for our H1N1 adjuvanted and unadjuvanted vaccine in almost 9,000 children, adults and elderly, ranging from 6 months to the elderly, including multiple trials being conducted under an FDA Treatment IND. The first clinical results were reported to HHS officials on September 4th and data on these trials is reported to HHS officials on an ongoing basis. These results helped inform government officials that a single 15ug dose was sufficient for most patients rather than two doses as previously thought. The FDA licensed our H1N1 vaccine for the U.S. market on September 15th. Novartis Vaccines also conducted clinical trials on an MF59 adjuvanted version of our U.S. H1N1 vaccine in anticipation of possible use of adjuvants in the U.S., which we had been preparing for though September.

- **H1N1 Vaccine Production.** H1N1 vaccine production in our Liverpool, England facility, which is dedicated exclusively to the U.S., was initiated in late July. We are currently operating our production facility with a very high level of quality and efficiency.

- **Opening of New Manufacturing Facilities.** Novartis Vaccines has expedited the completion of our new production facility in Liverpool, England, Site 4. This site was scheduled for opening at the end of second quarter of 2010, but we were able to accelerate validation of the facility by approximately 8 months to meet the volume of vaccine required by the U.S. Government. On October 9th, the FDA approved Site 4 and we are now manufacturing vaccine for the U.S. in this facility as well. Novartis Vaccines hired and trained 300 new employees in vaccine manufacturing and GMP so that the facility could be operational upon FDA approval.

- **Global Vaccine Development and Supply.** Novartis Vaccines has also successfully registered an adjuvanted egg based H1N1 vaccine (Focetria) and adjuvanted flu cell culture vaccine (Celtura) to supply countries across the globe. Clinical trials of our FCC

H1N1 vaccine, Celtura, were among the first clinical trials data available to government officials to determine formulation and dosage requirements of H1N1 vaccines.

- **Seasonal Vaccine Supply.** Novartis Vaccines delivered to the U.S. 27.1 million doses of seasonal influenza vaccine this season, only 400,000 doses less than we sold in the 2008-2009 influenza season. As of October 6th, we had completed our entire shipment of seasonal influenza vaccine to the United States, thereby providing more seasonal influenza vaccine earlier than at any other time in our history.

Voluntary Commitment of Liverpool Facility

Shortly after the declaration of the H1N1 pandemic, Novartis Vaccines worked closely with HHS to enter into an amendment to our pre-existing H5N1 supply agreement, entered into in September 2008, which provides a framework under which BARDA can purchase bulk antigen and adjuvant, as well as order storage and fill-finish of final vaccine to be delivered within 12 months of the order date.

At the same time we were agreeing to modify our pre-existing supply contracts, Novartis Vaccines faced the difficult decision of how to best utilize our Liverpool-based production facility. On the one hand, the U.S. Government had made clear that it would like the option to acquire all doses produced at the facility, but was not able at that time to commit to purchasing all doses produced in Liverpool nor to use adjuvanted vaccine. On the other hand, there was substantial global demand for vaccine and anticipated worldwide shortages, and Novartis Vaccines could likely quadruple our Liverpool dose output for global customers through adjuvantation. After consideration of our long-term partnership with the U.S. Government, Novartis Vaccines agreed to dedicate our entire Liverpool facility commercial production to U.S. vaccine needs. It is important to point out to the Committee that at the time Novartis Vaccines made this decision we had been in communication with more than 30 global governments to provide H1N1 vaccine. It would have been to our substantial business advantage to adjuvant our Liverpool supply to maximize global supply for an H1N1 vaccine (as another major manufacturer elected to do).

Seasonal flu production typically has a high degree of uncertainty due to many changing production variables. This uncertainty has been more extreme in this year's pandemic given the condensed production timeframe. At the time the U.S. Government ordered H1N1 vaccine, there were a number of uncertainties that Novartis Vaccines believed could impact production, including virus strain yield data, potency standards and formulation requirements to be utilized in H1N1 production. In light of these uncertainties, our contract with the U.S. Government included no fixed delivery dates by which any number of doses must be delivered. Instead, each task order includes conditional delivery dates that were based on certain stated assumptions and then current estimates applicable at the time of the order, and further, specific language was included regarding delivery timing that takes into account the unpredictable nature of vaccine manufacturing with a new and untested strain.

Accelerated H1N1 Production and Delivery

Novartis Vaccines has confronted multiple challenges and uncertainties in connection with our H1N1 pandemic efforts. To keep the government regularly informed, beginning in April, Novartis Vaccines has held weekly teleconference meetings with officials from four HHS agencies – Centers for Disease Control and Prevention (CDC), BARDA, FDA/CBER, and the National Institutes of Health (NIH) -- to review our supply forecasts and revised forecasts, clinical trial development, regulatory framework for approval of our H1N1 vaccine, production experiences with seed strains, reagent potency testing and shipping and distribution of vaccine. Novartis Vaccines has had to create and revise supply forecasts based on the most current information available to us, which have evolved over time. We have provided our forecasts to HHS on a weekly basis during these regular meetings, and they have reflected the impact on H1N1 vaccine supply of a number of issues unique to this year's pandemic, as described below:

- **Production Yields.** The initial seed virus supplied by government authorities resulted in extraordinarily low yields industry-wide in July when it was first used to produce H1N1 vaccine. For this reason, the initial government order for the vaccine assumed the 5 year average seasonal average yield and provides flexibility in delivery dates to account for the significant uncertainty that existed at the time. Yields did improve when a different seed virus was used but final yields were not known until FDA reagents and calibration values were available in August and then re-calculated in September. This led to changes in supply forecasts and stoppages in vaccine filling and ultimately affected the timetable for supply. In particular, the September re-calibration completed by regulators required Novartis Vaccines to stop fill-finishing activities for 8 days.

- **Egg Supply.** Orders for hens and eggs are generally placed 4-5 months prior to vaccine production to ensure healthy and appropriate sized flocks. Chicken farmers plan for this growth in farm size each Fall when contracts are engaged for egg supply for the following seasonal influenza season. For the H1N1 pandemic, egg supply for our Liverpool manufacturing site needed to be procured "out of season" in the late Spring and early Summer and contract farms needed to make unexpected adjustment in their flocks to provide eggs for 90 million doses of unplanned production, as well as to make adjustments in their planning to secure hens later in the Fall to assure an egg supply for the seasonal vaccine production required for the 2010-2011 influenza season.

- **Seasonal Production.** HHS prioritized seasonal influenza production, and at its request Novartis Vaccines completed seasonal vaccine production before switching to pandemic production. While this request helped to ensure that adequate supplies of seasonal vaccine were available early in the season, it left us less than 3 months to produce H1N1 vaccine prior to requested delivery.

- **Vaccine Formulation Decision.** Final direction on vaccine formulation became available in mid-August and final labeling in early September, delaying planning for executing fill and finish formulation and affecting the printing of the package inserts that accompany fill-finished vaccine.

- **Pre-Filled Syringes.** Although Novartis Vaccines indicated that we had limited pre-filled syringe formulation capacity, and therefore proposed to supply doses in multi-dose vials, the government ultimately requested a substantial part of our vaccine in pre-filled syringes. This affected our fill-finishing activities and the early availability of doses to the U.S public. Subsequently, based on HHS guidance, Novartis Vaccines prioritized multi-dose vials to accelerate the availability of finished vaccine.

- **Adjuvantation.** Although the government ordered bulk doses of our proprietary adjuvant MF59, which based on recently-available data could have quadrupled the number of doses supplied, it ultimately determined that use of the adjuvant was not warranted. Novartis Vaccines is currently providing only adjuvanted vaccine to all other regions of the world and believes that adjuvantation could have provided significant benefits to the U.S. in terms of supply volume for this year's pandemic.

As of November 16th, Novartis Vaccines has manufactured for the U.S. over 57 million doses of bulk antigen and over 61 million doses of bulk adjuvant and has shipped approximately 19 million fill-finished doses of H1N1 vaccine to the United States, of which almost 18 million doses are quality-released and available to supply HHS orders.

Given the totality of circumstances, the successful development, clinical testing, and large scale production of an H1N1 vaccine in such a short amount of time, despite all the challenges and uncertainties that were overcome, was a significant accomplishment for the U.S. Government and Novartis Vaccines partnership.

VI. Areas for the Future

We also believe, based on the experience this year, there are important opportunities to improve pandemic preparedness and response in the future, including the items described below:

- **Continued investment in new production technologies and manufacturing capacity including cell culture production.** Specifically, these investments should ensure production technologies and capacities enable the production of a wide range of influenza viruses and also ensure that these capacities can be brought on line quickly in the case of an influenza pandemic. Investment in technologies that support the rapid availability of vaccine candidate strains is also needed. During this pandemic there was a significant delay between the isolation of pandemic virus and the availability of vaccine candidate strains and too few laboratories were leveraged through the WHO Collaborating Centers to develop these seed strain candidates.

- **Acceleration of regulatory pathways for novel influenza adjuvants.** Novel adjuvants for influenza, such as oil in water emulsions like MF59, have been successfully used in Europe since 1997 both to provide dose sparing effects (and so allow the production of more doses in a limited amount of time) and improved cross protection (protection against drifted strains over a longer period). The licensure for these vaccines in the U.S. has not progressed due to the absence of a clear regulatory pathway.

- **Implementation of new methodologies for vaccine potency and sterility testing.** The analytical methods used to test vaccine potency and sterility are time consuming and often the rate limiting step to vaccine supply. The vaccine potency method, which involved the use of sheep antisera, often requires 8 weeks to develop for each new vaccine strain. During the current pandemic, Novartis Vaccines used a number of more modern methods to estimate vaccine potency which proved to be accurate. These methods are not currently accepted by regulatory authorities for vaccine batch release.

- **Streamlined regulatory approvals for pandemic vaccines including the use of mock-up filings.** The registration (before a pandemic occurs) of pandemic vaccines which requires only the submission of a strain change supplement after pandemic strain identification has streamlined the approval of pandemic vaccines in Europe.

- **Continued maintenance of the strategic national stockpile for rapid deployment.** Even the fastest and most efficient vaccine manufacturing technologies cannot produce vaccines within the first months of a pandemic outbreak and so are of little use when trying to contain the spread of pandemic virus. The establishment of a national stockpile of likely pandemic strains, along with adjuvant required to provide the protection against drifted strains, provides on opportunity to make vaccine available very quickly. To be most effective this vaccine needs to be held as filled, ready to use product.

In addition to the above areas, it is critical that the U.S. Government support seasonal influenza vaccination demand to ensure that suppliers are not forced out of the market if an oversupply situation arises as has happened repeatedly in the past.

Despite expanded recommendations in recent years, oversupply of seasonal influenza vaccines has lead to a downward trend in pricing. U.S. seasonal influenza manufacturing at 2008/2009 pricing levels was not profitable. This situation, combined with ever increasing regulatory requirements and additional data requirements for the licensure of new and improved influenza vaccine products, means that many improvements that could be made to ensure increased availability of vaccines in the event of a pandemic and to improve the efficacy of influenza vaccines in the U.S. are not being pursued.

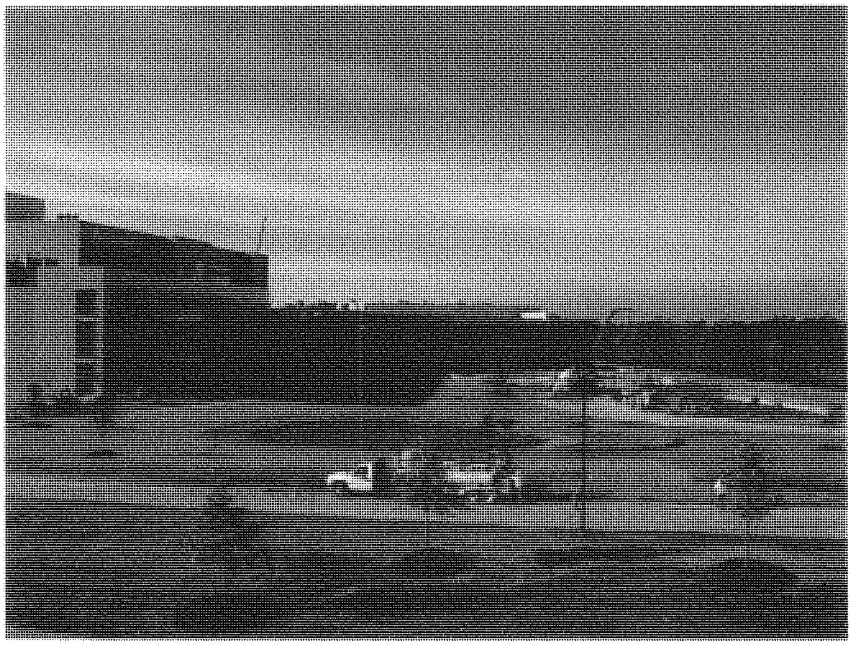
VII. Conclusion

Novartis Vaccines continues to do everything possible, in close collaboration with HHS, to maximize supply of safe and effective vaccine as soon as possible. We believe that when taken into full context the productive public-private partnership to produce, test, and deliver a safe and effective H1N1 vaccine to the U.S. has been a remarkable success. We are fully committed together with HHS to ensure we achieve our shared goal of preventing every possible case of influenza in the United States.

Thank you for the opportunity to present these views to the Committee. I will be happy to answer any questions that you may have for me.

Annex

Holly Springs Facility Photo



Schedule 7

Novartis Vaccines and Diagnostics, Inc. has received the following contracts from HHS since October 1, 2006:

Award Date	Contract Number	Description	Award Amount
April 1, 2006	HHSO100200600012C	Cell and Recombinant DNA Based Pandemic Influenza Vaccine	$220,507,491
November 15, 2006	HHSO100200700028I	Acquisition of Avian Influenza H5N1 Vaccine for the Strategic National Stockpile	$126,126,000
January 17, 2007	HHSO100200700030C	Advanced Development of Antigen Sparing Pandemic Influenza Vaccines	$100,045,857
September 22, 2008	HHSO100200800072I	Acquisition of Influenza H5N1 and H1N1 Vaccine for the Strategic National Stockpile	$1,048,338,833
January 15, 2009	HHSO100200900101C	Building Domestic Cell-based Influenza Vaccine Manufacturing Facilities	$486,579,000

Mr. STUPAK. Thank you Doctor.

Dr. Machielse, your testimony please. Turn that green light on and pull it forward. Thank you.

TESTIMONY OF BEN MACHIELSE

Mr. MACHIELSE. Chairmen Stupak and Pallone, Ranking Members Walden and Deal, members of the committee, thank you for the opportunity to address you today.

My name is Ben Machielse. I'm the Executive Vice President of Operations for MedImmune, and I'm also chairing the MedImmune's H1N1 preparedness committee.

MedImmune has changed the landscape of influenza vaccination when we launched FluMist in 2003, representing the first innovative development in flu vaccines in over 60 years. This year, MedImmune has contracted with BARDA to deliver nearly 42 million doses of intranasal vaccine based on our FluMist technology. Between September, 2009, and February, 2010, we plan to deliver those doses.

The 42 million doses of H1N1 vaccine, along with fulfilling our commitment of 10 million doses of seasonal vaccine, represent an increase of 700 percent in MedImmune's vaccines production compared to last season. Importantly, MedImmune's manufacturing for H1N1 had no impact on our commitment to deliver 10 million doses of seasonal vaccine. In fact, we were able to accelerate seasonal delivery and we delivered the first H1N1 vaccine this season to BARDA.

Due to manufacturing efficiencies and high vaccine yields unique to our technology, the intranasal vaccine was the first available and remains a significant proportion of the vaccine available to date. We have finished the manufacturing of all 42 million bulk doses of vaccine, all of which is now on U.S. soil. We are now in the process of filling the vaccine in the specialized single-dose nasal sprayers. As of Friday, November 13th, we have shipped approximately 13.2 million doses and are over 96 percent on track with delivering the orders BARDA has placed.

MedImmune's unique technology provided the significant search capacity for both vaccines. This success validates MedImmune's technology as a strategic asset in pandemic preparedness.

As a result of MedImmune's excess bulk vaccine we have submitted a proposal to BARDA regarding an alternative delivery device in order to further contribute to public health effort.

The development and manufacturing process for our intranasal vaccine differs from that of the shot in several important ways. We develop our own unique master virus seed to grow the vaccine, while most of other manufacturers rely on CDC or other reference labs to generate the master virus seed.

Critical to pandemic preparedness efforts is that we use a patented technology known as reverse genetics to rapidly create multiple strains and then we can select one that grows well in eggs and has the other necessary properties, too. Like the shot, our vaccine is also produced in eggs. However, unlike the shot, we generate between 60 and 100 doses of vaccine per egg.

Longer term, replacing egg-based technology cell culture manufacturing would be a key advancement for influenza vaccines. In

fact, we believe that cell culture technology used to manufacture intranasal vaccine will have similar yield advantages as to the one I mentioned in the egg-based technology.

MedImmune has an R&D program focused on the development of the cell-culture-based vaccine. However, FDA requirements have increased the cost and duration of the development program by several years, and this program is now on hold while MedImmune and HHS evaluate the appropriate path forward.

Now is the time to collectively evaluate what we have accomplished and what we can do better. It is critical that the U.S. government continue to encourage a high level of seasonable vaccination as well invest in public education campaigns that increase awareness of the benefits and options in influenza vaccination.

Additionally, it's key that government agencies and industry jointly develop a blueprint for processes and requirements across a number of key areas, including, for example, clinical development, regulatory requirements, and distribution, to avoid any roadblocks that could delay delivery of vaccine in the future.

In the few years that BARDA has been in existence, we believe they have done a remarkable job. MedImmune is pleased to be delivering intranasal vaccine in line with BARDA's expectations, and we look forward to building up our successful relationship in collaboration with the U.S. Government.

I will be pleased to answer any questions.

[The prepared statement of Mr. Machielse follows:]

STATEMENT OF BEN MACHIELSE, DRS.

EXECUTIVE VICE PRESIDENT, OPERATIONS

MEDIMMUNE

BEFORE THE HOUSE ENERGY AND COMMERCE
SUBCOMMITTEE ON OVRSIGHT AND INVESTIGATIONS AND
SUBCOMMITTEE ON HEALTH

"CURRENT STATE OF VACCINE AVAILABILITY AND
THE NEXT STEPS IN PRODUCTION AND DISTRIBUTION
EFFORTS"

NOVEMBER 18, 2009

Joint Hearing of the Subcommittee for Health and the Subcommittee for Oversight & Investigations of the House of Representatives Energy & Commerce Committee

Testimony of Ben Machielse, Drs., MedImmune

Joint Hearing of the Subcommittee for Health and the Subcommittee for Oversight & Investigations of the House of Representatives Energy & Commerce Committee

November 18, 2009

Testimony of Ben Machielse, Drs., MedImmune

Chairmen Stupak and Pallone, Ranking Members Walden and Deal, Members of the Committee, thank you for the opportunity to address this joint hearing of the Subcommittees of Health and Oversight and Investigations.

Overview

My name is Ben Machielse, and I am executive vice president of operations for MedImmune and also the chair of MedImmune's H1N1 response team. By way of introduction, MedImmune is a biotechnology company wholly owned by AstraZeneca, PLC. MedImmune is headquartered in nearby Gaithersburg, Maryland, and is committed to delivering life-changing products and improvements in patient health. As part of that mission, we pioneered the first major innovation in influenza vaccine development in almost 60 years with the 2003 launch of the intranasally delivered seasonal FluMist®, the first (and still the only) live, attenuated influenza vaccine approved by the FDA.

We are now in our seventh season as a licensed manufacturer of a commercially available influenza vaccine. This season has been unlike any other we have been through with the outbreak of the 2009 novel influenza A/H1N1 virus. As you well know, President Obama has declared a national State of Emergency and the World Health Organization has declared a global pandemic. Influenza pandemics are not new, having occurred every few decades during the 20th century.

What is new is that, for the first time, we have advancements in place to protect ourselves against a pandemic, thanks in large part to a successful collaboration between the private sector and the U.S. Department of Health and Human Services (HHS).

Since 2006, MedImmune has been working with the Biomedical Advanced Research and Development Authority (BARDA) in the Office of the Assistant Secretary for Preparedness and Response within HHS on pandemic preparedness efforts. This year MedImmune contracted to deliver nearly 42 million doses of our intranasal live, attenuated H1N1 vaccine to HHS/BARDA for delivery to the U.S. public between September 2009 and February 2010.

Today I am pleased to share that we are on schedule to fulfill the terms of this contract to provide pandemic vaccine to the American population. The FDA released over 13 million doses of our finished sprayer-filled H1N1 vaccine as of Friday, November 13, 2009, and our schedule for delivery of finished product through the end of February remains on track and consistent with BARDA's expectations. We have finished the bulk manufacturing of all 42 million doses of the vaccine ahead of the schedule agreed upon with BARDA. All of the vaccine material is here on U.S. soil, and we are now in the process of filling the vaccine into the specialized single-dose nasal sprayers we use for delivery of our vaccine. I am also pleased to report that MedImmune was the first of the five influenza vaccine manufacturers contracted by HHS to deliver an H1N1 vaccine this year. We did so three days ahead of schedule on September 22, 2009. As a result, our vaccine was the first available for the U.S. public and has been used in the H1N1 vaccination campaign to help protect priority populations including health care workers, first responders and eligible children and young adults between the ages of 2 and 24. Our product remains a significant proportion of the vaccine supply available to date.

I believe it is also important for the Members of the Subcommittees to be aware that there was no disruption of our seasonal influenza vaccine manufacturing or delivery due to our work on the H1N1 vaccine. When we began work on the H1N1 vaccine, we also accelerated our manufacturing processes to ensure that our commitment to make approximately 10 million doses of seasonal vaccine was met.

Manufacturing

I understand that the Members of the Subcommittees have questions about our manufacturing process, so I will provide a brief overview. As the manufacturer of the only live, attenuated influenza vaccine in the U.S. as well as the only influenza vaccine administered by nasal spray rather than a shot, our manufacturing process differs from that of the inactivated, injectable vaccine in several important respects.

First, we have a highly specialized and dedicated vaccines research and development team that every year develops a special "master virus seed" for every strain to be included in the vaccine for the upcoming influenza season. I understand the other influenza vaccine manufacturers rely on the CDC or other reference laboratories around the world to generate the necessary master virus seed, which makes our team in Mountain View, California, one-of-a-kind in the industry. This year, our team had completed their work for the 2009-2010 seasonal FluMist vaccine and was working on other projects when the H1N1 outbreak was first identified at the end of April. We immediately invested our own resources and reassigned this expert team of influenza vaccine scientists to begin work on an H1N1 vaccine seed due to the emerging and unpredictable public health threat.

Our team uses a patented process known as "reverse genetics" or "plasmid rescue" to first select those parts of the H1N1 virus that will stimulate an immune response and then harness them to a special, proprietary vaccine strain. This specialized strain is "live" when it is administered, in that it has been adapted to grow in the cooler temperatures of the nose (which allows for generation of an immune response), but "attenuated" and "temperature sensitive" which means it cannot survive in the warmer body temperature of the lungs (so it cannot cause influenza). This reverse genetics process allowed our team to quickly make 23 different candidate master virus seed variants before identifying that one which exhibited the best attributes, including good growth in chicken eggs necessary for vaccine production. This master virus seed was sent to our egg-based bulk vaccine manufacturing plant in the United Kingdom at the end of June. In parallel to this H1N1 development activity, we accelerated and completed the production of the seasonal bulk vaccine to allow for the start of bulk H1N1 vaccine manufacturing on July 3, 2009.

Like the inactivated vaccine of our competitors, our vaccine is grown in eggs. However, unlike the inactivated vaccine, which typically generates only one to seven doses per egg, we find that live, attenuated vaccine strains can generate between 60-100 doses of vaccine per egg. This year the live, attenuated H1N1 master virus seed has been no exception, allowing us to generate approximately 90 doses of vaccine per egg. The high yields of the live, attenuated vaccine are a direct result of MedImmune's ability to prepare multiple candidate seeds using reverse genetics and then selecting the seed that has optimal performance properties in our manufacturing process. Because MedImmune's vaccine is live and grows in the nose where it activates an immune response, much less virus is required to be given in comparison to the

injectable vaccine. In the height of the seasonal vaccine production cycle we normally manufacture two bulk vaccine lots per week, but given the public health emergency, we have added over 40 people to our bulk vaccine manufacturing labor force, and stretched manufacturing capacity by running three lots per week on average.

Finally, all the bulk vaccine is shipped from our UK facility to our facility in Pennsylvania where we fill the vaccine into sprayers and finish the packaging process. We have also augmented staff at this site to fill and finish product on a 24/7 basis and have suspended manufacturing activities at our primary non-vaccine manufacturing facility to focus on our H1N1 efforts.

I would also like to highlight that in 2007, MedImmune contracted with BARDA to retrofit existing facilities to prepare for a surge in case of a pandemic. Part of that effort included development of a second high-speed, FDA-approved fill line in our Pennsylvania facility that was scheduled to be completed by June 2010. Fortunately, this project was far enough along that we were able to accelerate its development by seven months. Obtaining early licensure for this second high-speed fill line in service has been critical for us to continue to deliver H1N1 vaccine on the schedule agreed upon with BARDA. We received extraordinary support from the FDA to accelerate the process and I am pleased to announce that this fill line was officially licensed Friday, November 13, 2009.

I would also like to recognize the efforts of the team in our distribution facility outside Louisville, Kentucky. This site is generally used for storage and distribution of our products. However, last-minute changes required by the FDA for the package insert for the H1N1 vaccine meant that approximately 40 staff members at the Louisville facility worked in double shifts for

six weeks in the minus 40 degree Celsius temperature freezers in which the product is stored to ensure that the correct package insert was included with the vaccine.

The men and women of MedImmune are honored by the trust placed in us by the U.S. Government and humbled by our responsibility to the U.S. public. I am proud of the dedication and commitment shown by the MedImmune team that has allowed us to continue to deliver vaccine as contracted. That is not to say that there have not been challenges, but in each case, the team has been able to find a way to minimize the impact of any disruptions to our delivery schedule. We are on pace to deliver nearly 42 million doses of H1N1 vaccine this season in addition to the 10 million doses of seasonal vaccine we have already distributed. Combined, this means we are on track to complete a 700% increase over the seven million doses of seasonal vaccine we delivered for the 2008-2009 flu season. We believe this to be a tremendous accomplishment and speaks to the company's commitment and ability to respond intelligently and quickly to a public health emergency. Yet, we also recognize that while we are meeting our commitments to BARDA, that fact is of little comfort to those members of the public who have not yet obtained vaccine. It is with this in mind that we have continued to push our teams to see if there are any parts of the process we can further accelerate to deliver product even sooner. Given the overall vaccine supply shortage, we have also been working with BARDA to determine if there are other steps we can take to safeguard public health both for the remainder of this season and the future. I would like to take a few minutes to inform the Subcommittees of our latest thinking in that regard.

New Approaches

Joint Hearing of the Subcommittee for Health and the Subcommittee for Oversight & Investigations of the House of Representatives Energy & Commerce Committee

Testimony of Ben Machielse, Drs., MedImmune

Multi-Dose Vials with Disposable Nasal Droppers

MedImmune's capacity for bulk production of live, attenuated vaccine significantly exceeds our ability to acquire the specialized sprayers and fill them, particularly in the context of a pandemic when a rapid surge of vaccine supply is quickly needed. When we realized in late July and August that we had the capability to produce more than enough bulk vaccine to meet our commitments to HHS, we began discussing with BARDA and the FDA the possibility of filling our vaccine into vials that would contain multiple doses of vaccine and distributing them with single-use disposable nasal droppers. At that time, we proposed an aggressive schedule to deliver 30 to 50 million more doses in October in this multi-dose presentation. However, we slowed our development efforts in September when BARDA believed there would be enough injectable vaccine forthcoming, particularly in light of clinical data showing one dose of injectable vaccine would be sufficient for most Americans over nine years of age.

Although it would likely be the end of January or early February 2010, before we could have doses available in this multi-dose presentation, we believe it is important to pursue this development program with renewed vigor for two reasons. First, while no two pandemics have been the same, history has shown that there can be multiple waves of infection and the length of each wave can vary. If the current wave continues for a prolonged period or another wave occurs early next year, this approach would provide additional quantities of vaccine to augment the sprayer-filled doses we are currently providing, particularly if the delays with injectable vaccine delivery continue. Second, historically, the influenza virus has shown a remarkable ability to mutate, but we have no way of predicting how and when it might. If it mutates enough in 2010 that current H1N1 vaccines do not provide sufficient protection, it may be necessary to

rapidly create a novel vaccine against the mutated strain. In such a circumstance, MedImmune believes we could use the same technology used this year to rapidly create a high-yielding vaccine strain. However, the limited supply of sprayers could delay ability to deliver vaccine. The multi-dose vial and disposable dropper solution we are proposing, however, would alleviate sprayer supply constraints, allowing for a significant surge in 2010 or in future pandemics. For these reasons, we believe this solution holds strategic importance for pandemic preparedness both in the near-term and in the long-term.

A key factor for this approach will be determining if the FDA has the resources to evaluate and grant regulatory approval for the multi-dose vials and disposable droppers in time to release product in January or February. Fortunately, several of the early clinical trials of seasonal FluMist used droppers rather than sprayers, providing us with existing clinical data showing that nasal drops are an equivalent alternative. One existing procedural hurdle is that current regulations constrain the FDA's ability to evaluate the safety and efficacy of multi-dose vials of vaccines that do not contain preservatives. MedImmune's vaccine is preservative-free. It is our scientific opinion that this regulation was intended to cover injectable vaccines and is not as critical for vaccine administered into the nose, which is not itself sterile. This position is supported by the United States Pharmacopeia guidance for intranasally administered pharmaceutical products. Without modernizing FDA's evaluation process, we are concerned that introducing preservatives could affect a live, attenuated intranasal vaccine in unanticipated ways. Initial studies have indicated that a preservative is not necessary. In addition, the time required to test the product with a preservative would significantly delay the timeline for availability of vaccine in the multi-dose vial presentation. These same FDA regulations also

contain an exception to the preservative requirement for yellow fever vaccine, providing a precedent for producing vaccine in multi-dose vials without preservatives, but the standard procedure required for FDA rulemaking would also delay delivery of vaccine, even if the agency concurs with our scientific position and supportive data.

As previously stated, we have been in an on-going dialogue with the FDA and BARDA regarding this approach and are hopeful that our approach can be added to the pandemic preparedness arsenal.

Cell Culture-Based Vaccine

While licensure of seasonal FluMist by the FDA was a significant milestone in influenza vaccine innovation, we view this as not the culmination of our work, but rather a step along the evolution of this important vaccine. MedImmune continues to seek out and develop improvements that will help more people get access to this vaccine well in advance of the first waves of influenza disease. While not a possibility for the current H1N1 pandemic, replacing dated technologies with a modern cell culture manufacturing system would be a key improvement for the development of this vaccine. Cell culture manufacturing offers many advantages compared to egg production. Among these advantages are the protection of the vaccine from external contaminants, and the scalability of production. A typical production run of our live, attenuated vaccine uses 30,000 eggs, each of which must be individually handled to extract the vaccine from it, yielding approximately two to three million doses of bulk vaccine. In contrast, two moderately sized bioreactors could yield more than one hundred times that amount of bulk vaccine and require significantly less handling. Cell culture production, therefore, is less

labor intensive and produces more vaccine per unit of time. Conversely, increasing the scale of egg-based production requires a coordinated increase in both the number of eggs as well as the number of hens to lay the eggs. This egg-based system is inflexible, could take more than a year and result in a substantial increase in the number of eggs. The egg-based system is also susceptible to viruses that affect the hens or the eggs such as the H5N1 "avian flu" virus that was identified a few years ago. Such a virus could significantly deplete the number of hens and eggs, reducing the supply of eggs required to create the vaccine. In contrast, cell culture production is limited only by the number of available bioreactors, standard equipment throughout the biotech industry. Current estimates predict that MedImmune could produce hundreds of millions of doses of bulk vaccine within six months with only two mid-sized bioreactors. Increasing this output would require only modest investments in equipment and facilities compared to an egg-based approach.

MedImmune understands the importance of protecting the U.S. population from influenza and, as a result, there is a clear and compelling need to advance beyond egg-based manufacturing to cell culture production technology. The company currently has a research and development program focused on developing a cell culture-manufactured live, attenuated vaccine and has performed this work under a contract with BARDA since 2006. Key components of successfully incorporating changes for any product are identifying, characterizing and managing potential risks associated with the changes. MedImmune's initial contract for cell culture-produced live, attenuated vaccine examined the key risks of the program and set forth a series of studies to evaluate the magnitude of these risks. The genetic elements of the vaccine are identical between the cell-produced and egg-manufactured products, and we therefore determined that there was

little risk that the effectiveness of the vaccine would be different. We proposed to directly assess this by evaluating the immunogenicity of the two products side-by-side in human studies.

In September 2008, the Vaccines and Related Biological Products Advisory Committee, a body of scientific experts convened by the FDA, supported initiation of human clinical studies. However, the FDA determined that additional studies would be required which substantially increased the cost and duration of the development program by several years. In light of these changes, the program remains at a late preclinical stage and would unlikely be licensed in a similar population as indicated for FluMist within the next five years. The program no longer fit the original expectations of the contract and is currently on hold while MedImmune and HHS discuss an appropriate path forward. Our egg-based live, attenuated technology has proven to be a very important asset in the pandemic preparedness program in terms of its yield and speed to market. These advantages translate directly to the cell culture technology presenting a clear and urgent need to define an efficient approval process.

Manufacturers urgently need a way to discuss end-to-end product development plans with the FDA or its advisory boards early in the product development process. We must work together towards efficient, meaningful science-based outcomes that move medicines forward. In the current environment, the hurdles to bringing forward innovative products like cell culture-produced live, attenuated influenza vaccines are likely to take many years and cost a great deal. Measurement of infrequent events is better managed by improved post-marketing tools. It would be unfortunate to not have available, technology with large-scale production capabilities in place in advance of the next pandemic. Cell culture-produced live, attenuated vaccine can and should be a cost-effective, fast and reliable part of the U.S. pandemic preparedness program.

The events of 2009 have reinforced the need for a strong public-private partnership to advance influenza vaccine manufacturing and development. For cell culture manufacturing to become a reality for pandemic and seasonal influenza vaccine, manufacturers, regulatory agencies and public health agencies of the U.S. government must work in concert to make these important advancements a reality.

Blow-Fill-Seal Technology

While we are on track to increase our vaccine production by 700% this year, it is clear that availability of the sprayers and the speed at which they can be filled can be rate-limiting when a significant surge in production is required. Accordingly, MedImmune has also been developing a new method of delivering our live, attenuated vaccine in a more cost and time-efficient manner. Such a method would eliminate our current dependence on sprayers. This technology, referred to as "blow-fill-seal," would allow for rapid mass filling of the bulk vaccine into plastic bulbs and is currently being studied in clinical trials at MedImmune. Based on the feedback we have received from the FDA to-date, we believe that vaccine in this presentation may be available in three to five years.

Looking Ahead

While our strong collaborative efforts with the U.S. Government have allowed us to respond well to this public health challenge, we have already explored what we can do better the next time a pandemic threat emerges. There are many opportunities to continue to develop the

science and capacity needed to enhance our pandemic vaccine preparedness for potentially even more serious outbreaks.

First, there is a very strong correlation between a manufacturer's seasonal influenza vaccine capacity and the ability to produce an adequate supply of pandemic vaccine. As demand for seasonal vaccine increases, manufacturers respond with more supply and are more prepared to meet the demands of a pandemic. In order to ensure that manufacturers have the capacity to produce an adequate supply of pandemic vaccine, it is critical that HHS and CDC continue to encourage increased seasonal vaccination in all recommended populations. Influenza vaccines are safe, effective and among the most cost-effective medical interventions available. By significantly increasing the annual use of seasonal vaccines we could improve health, reduce health care costs, diminish the impact on the economy from missed days of work and establish the manufacturing capacity and distribution systems necessary to respond adequately to protect all Americans when the next pandemic strikes.

Second, there are many misconceptions about the risks of vaccination, including a lack of understanding of its benefits and of the scientific and medical data supporting the vaccine. For example, the safety of our live, attenuated vaccine has been demonstrated in numerous human clinical studies and reconfirmed annually by testing one dose per patient in approximately 300 adults before that year's vaccine is approved by the FDA. For this year's H1N1 vaccine, at the FDA's request, we went ever further and tested two doses per patient in approximately 300 adults and 300 children. We would strongly encourage a substantial investment in education campaigns that would provide the public with the appropriate scientific information on influenza vaccines. With our focus on innovation, we would be particularly interested in making sure that

any such public awareness and education campaigns, particularly those that are government-sponsored, go beyond the "flu shot" language that is currently used to instead discuss the "flu vaccine" more generally so they are inclusive of the live, attenuated vaccine, as well as address the ease and simplicity of nasal delivery and other technological enhancements that have come to the forefront.

As stated before, while there are delays in injectable vaccine availability, this is the first pandemic in history in which vaccine manufacturers have been able to develop and mass-produce a vaccine within the same season that the pandemic strain first circulated. BARDA has done a remarkable job of establishing a plan to vaccinate the American public and coordinating related efforts of public health agencies and private industry. While the decision-making process and speed of response have been much faster than usual, we do believe that rapid responses to emergency situations would benefit from collaborative advance scenario planning. Both manufacturers and regulatory decision makers can learn lessons from this pandemic to minimize the risk of future vaccine supply delays and disruption.

Finally, we believe it is important that Congress continue to fund pandemic preparedness efforts not just at BARDA, but also to ensure that other key agencies, such as the FDA and CDC have the necessary resources.

Conclusion

MedImmune is fully committed to and engaged in assisting the U.S. government in its efforts to protect public health during this challenging time. We have, to date, successfully executed against an aggressive schedule and believe we can continue to so. We believe we have

an exceptional team in place to handle this H1N1 influenza pandemic and continue to benefit from excellent input and collaboration with HHS. It is our continuing honor and privilege to be able to serve the country during this national emergency.

I would like to again express thanks to the Subcommittees on behalf of MedImmune and our parent company, AstraZeneca for the opportunity to testify today. I hope this information has been useful and I am pleased to answer any questions from Members of the Committees.

Mr. STUPAK. Thank you, Doctor.
Mr. Hosbach, your testimony please.

TESTIMONY OF PHILLIP HOSBACH

Mr. HOSBACH. Good afternoon, Mr. Chairman. Thank you for the opportunity to testify before the subcommittees regarding H1N1 influenza pandemic production development and delivery.

My name is Phil Hosbach. I am the Vice President of Immunization Policy and Government Relations for Sanofi Pasteur, and I am currently responsible for coordinating the company's worldwide and U.S. Pandemic response teams.

Sanofi Pasteur is the largest manufacturer of influenza vaccine globally and in the United States, producing about 45 percent of the U.S. annual influenza vaccine supply. We are the only manufacturer of an activated flu vaccine on U.S. soil, and all of our seasonable and H1N1 vaccines for the U.S. market are produced in Swiftwater, Pennsylvania. This site, which includes two state-of-the-art influenza vaccine manufacturing facilities, and one of those was just licensed this year, as you heard from Dr. Goodman, they are operating 24 hours a day, 7 days a week, with more than 2,000 dedicated people involved in some way in getting the vaccine out the door. Many of these people have made great personal sacrifices to ensure that we produce the largest number of H1N1 vaccine doses in the shortest amount of time while ensuring vaccine safety and regulatory compliance.

I would like to start my remarks today by focusing on what a remarkable achievement the U.S. response to this pandemic really is. Thanks to the close collaboration of industry with HHS, FDA, and CDC, we are better prepared for this pandemic than we would have been at any other time in history.

The virus was identified in late April. Manufacturers received the seed strains from CDC in late May. Less than 4 weeks later, large-scale manufacturing was initiated; and by late October there was an FDA-approved vaccine being administered.

It truly is a success story. Nevertheless, we certainly understand the committee's interest in this process, as there are always opportunities to improve.

Sanofi Pasteur began shipping H1N1 vaccine on September 29th, which was earlier than anticipated. We have received orders from HHS for 75.3 million doses of bulk antigen to be delivered by the end of the year. We will meet this commitment.

While Sanofi Pasteur represents only 75 million doses of the 250 million doses purchased by HHS, I am proud to say we represent almost 50 percent of what has been delivered to CDC to date. Sanofi Pasteur has largely succeeded in producing the H1N1 vaccine as initially projected. However, there were some factors that impacted even our considerable abilities and extensive preparation.

The most significant factor initially was the lower-than-expected production yield for the seed strain. It is an unfortunate fact of Mother Nature, but we sometimes see lower-yielding strains even for seasonal flu. However, the initial yields for H1N1 were exceptionally low. Utilizing our expertise, we have been able to optimize the productivity of the seed virus. Our current H1N1 yield should not be a significant factor going forward.

Since April 30th, we have participated in weekly phone calls with HHS agencies, including BARDA, CDC, FDA, and NIH, during which we provided ongoing updates. We have always been transparent about our progress. We now project that we'll not only catch up completely but we may even be ahead of schedule in the coming weeks.

The media coverage regarding H1N1 vaccine shortages have spurred some to question whether the egg-based manufacturing technology might be outdated. The egg-based vaccine production method we currently used has seen many technological advancements and is a very sophisticated process that has proven adaptable to emergency situations like the current pandemic. In fact, this year provides us with an opportunity to directly prepare the availability of flue vaccines prepared with egg-based technology and those produced in Europe using cell culture. In the end, each of the methods used produce clinical lots within similar time frames; and large-scale production was initiated at nearly the same time.

Contrary to popular perception, cell culture is not a new vaccine production process. It's been around about 25 years and does not save substantial time when it comes to producing influenza vaccine. It does not produce a safer or more effective vaccine and does not necessarily increase yields, which was a critical variable this year.

The production of an influenza vaccine involves many steps, many of which are the same regardless of the technology or medium used. For example, growing antigen or any medium can only begin after the seed virus is isolated and is sent to manufacturers by CDC. Following no matter which production method is used, all vaccines must undergo rigorous quality control and safety testing. This testing accounts for approximately 85 percent—and I repeat—85 percent of the production time.

This year, Sanofi Pasteur faced the unprecedented and complex challenge of producing two influenza vaccines simultaneously. I am proud of the work of our people, that our people have done in ensuring that Sanofi Pasteur will not only meet its commitment to deliver 75 million H1N1 doses to HHS but also meet its promise to deliver all 50 million doses of seasonal vaccine to its customers before the peak of the annual flu season. It is important to note that we still have a very long flu season ahead of us.

Again, it is a credit to all involved that we have been able to respond as well as we have to this pandemic. While it is important and appropriate to discuss where improvements can be made, I believe it is equally important to recognize the accomplishments.

Mr. Chairman, thank you again for allowing me the opportunity to testify; and I look forward to any questions.

[The prepared statement of Mr. Hosbach follows:]

sanofi pasteur
The vaccines division of sanofi-aventis Group

Written testimony of

Phil Hosbach

Sanofi Pasteur Inc.

Before the

House Committee on Energy and Commerce

Subcommittees on Health and Oversight and Investigations

November 18, 2009

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Sanofi Pasteur Inc.

Written testimony of Sanofi Pasteur Inc. submitted to the House Committee on Energy and Commerce Subcommittees on Health and Oversight and Investigations November 18, 2009

On behalf of Sanofi Pasteur, I would like to thank you for the opportunity to testify before the Subcommittees regarding a vital public health issue: the H1N1 influenza pandemic. As the world's largest and most experienced manufacturer of influenza vaccine, Sanofi Pasteur is committed to working in close cooperation with US and worldwide authorities to develop, produce and distribute a safe and effective Influenza A (H1N1) vaccine.

I. Background

Sanofi Pasteur is the largest company in the world devoted entirely to vaccines. Sanofi Pasteur offers the broadest range of vaccines protecting against 20 infectious diseases. In 2008, the company provided more than 1.6 billion doses of vaccine, making it possible to immunize more than 500 million people across the globe.

Sanofi Pasteur employs more than 11,000 employees worldwide and more than 3,200 here in the US. We have major facilities in Lyon, France, Toronto, Canada and Swiftwater, Pennsylvania. The Pennsylvania site is one of the company's four major integrated vaccine research and manufacturing centers. The site includes activities in research and development, production, filling and packaging, and distribution.

Sanofi Pasteur is the largest and most reliable manufacturer of influenza vaccine in the US and abroad, producing about 45 percent of the US annual influenza vaccine supply and about 40 percent of the worldwide supply. We are also the only domestic manufacturer of inactivated, injectable influenza vaccine. We have two licensed influenza vaccine manufacturing facilities

operating in Swiftwater, the second of which was licensed on May 6, 2009 by the Food and Drug Administration (FDA) and represents a 140,000-square-foot, $200 million corporate investment by Sanofi Pasteur in domestic influenza vaccine manufacturing capacity, as well as a commitment to job creation in Pennsylvania. When running at full capacity, this new facility should produce approximately 100 million doses of the three-strain seasonal influenza vaccine per year. The original facility in Swiftwater is capable of producing 50 million doses of the three-strain seasonal influenza vaccine per year. Both facilities have been used to produce both seasonal and H1N1 vaccines and are now fully dedicated to H1N1 vaccine production. All seasonal and H1N1 vaccines for distribution by Sanofi Pasteur in the US are produced in Pennsylvania.

II. Pandemic Preparedness

Sanofi Pasteur has a long history of working collaboratively with both US and worldwide public health authorities on pandemic influenza. In 2004, we began working with the US Department of Health and Human Services (HHS) on early planning for a pandemic. We were the first to develop a proven large-scale manufacturing process for the H5N1 avian influenza vaccine, and we remain the only licensed manufacturer for H5N1 vaccine in the United States. Though at that time the focus was H5N1, otherwise known as bird flu, the groundwork laid has proven critical to our response to the H1N1 virus. For example, one of the most important steps toward preparing for an influenza pandemic was to put continuous egg supply contracts in place for vaccine producers. This has allowed the company to manufacture influenza vaccine on a year-round basis.

Unprecedented collaboration between industry and government has also been a hallmark of current pandemic response efforts. Sanofi Pasteur and all of the public health government agencies (HHS, FDA, BARDA, CDC and NIH) have worked to develop and produce a vaccine as rapidly and carefully as possible. Since April 30, 2009, Sanofi Pasteur has participated in weekly conference calls with these agencies in order to coordinate and plan for the testing, production and distribution of the H1N1 vaccine produced in Swiftwater. This collaborative approach can be credited with some early successes. For example, through close coordination with FDA and HHS, we were able to accelerate the licensure of two new filling lines in the new Formulation and Filling Facility at our Swiftwater location - one of which was not scheduled to be licensed until next year. Both lines are now operational and providing additional filling capacity. Licensure of a third line is pending, also on an expedited basis.

While the current H1N1 pandemic response has revealed key areas for improvement in public health infrastructure, our government agencies deserve recognition for their foresight and tireless effort in responding to the current pandemic. Sanofi Pasteur is committed to continued collaboration with key public health agencies and to remaining a consistent and reliable manufacturer of vaccines.

III. Production

Sanofi Pasteur's goal is to produce the largest number of H1N1 vaccine doses in the shortest amount of time while ensuring vaccine safety and compliance with the legal and regulatory requirements of public health authorities. (See Exhibit A for vaccine development process.) We have been working in close cooperation with key US government agencies including HHS, CDC, FDA, NIH and BARDA to accomplish this goal. We have devoted

extraordinary resources to the production of both seasonal and H1N1 vaccine this year. Today, more than 2,000 people at our Swiftwater facilities are in some manner involved responding to the pandemic through development, production, testing and distribution of the H1N1 vaccine. Our production facilities are running at their full licensed capacity, 24 hours a day, 7 days a week, with many of our employees making exceptional personal sacrifices to develop, produce and deliver vaccine as quickly and carefully as possible.

We have moved quickly to produce the vaccine to meet demand, but have taken no shortcuts. Sanofi Pasteur expects to produce and distribute over 125 million doses of influenza vaccine this fall in the United States– 50.5 million seasonal and 75.3 million doses of H1N1 vaccine.

IV. Egg-Based Technology

This level of production is achieved by employing a proven, well-tested method that uses egg-based technology. Recent reports of H1N1 vaccine shortages have spurred some to question whether the egg-based manufacturing technology might be out-dated. Ironically, it is largely because the vaccine manufacturing process is so well-established that the vaccine's safety profile is so well defined. Contrary to popular perception, cell culture technology does not necessarily increase yields and there is no evidence that cell culture derived vaccine is more efficacious than egg-derived vaccine.

Historically, chicken eggs have provided the most advantageous and reliable method for producing influenza vaccine. More than 95 percent of the world's influenza vaccine production uses egg-based technology and this method is anticipated to provide the majority of the world's

influenza vaccine for the foreseeable future. Currently, there are no cell culture H1N1 influenza vaccines licensed in the US.

The egg-based vaccine production method we currently utilize is a technologically sophisticated process that has proven adaptable to emergency situations like the current pandemic. In fact, this year provided us with an opportunity to directly compare the availability of influenza vaccines produced with egg-based and European cell culture-based production for a novel pandemic strain. Each of the methods produced clinical lots within similar timeframes. Large-scale production was initiated in nearly the same timeframe. More importantly, the US was the first country to start a nationwide influenza immunization program, receiving all of its vaccine from egg-based production.

The production of an influenza vaccine is a complicated process, involving many steps that typically take about six months to complete from the time a seed virus is received. Many steps in the process are the same regardless of the technology used. For example, growing antigen on any medium can only begin after the seed virus is isolated and is sent to manufacturers by the US Food and Drug Administration. Additionally, no matter which production method is used, all vaccines must undergo rigorous quality control and safety testing. This testing is done for each individual vaccine production lot and accounts for approximately 85 percent of the production timeframe. The testing is comparable for both egg-based and cell-culture technologies.

V. Timeline Delays

As mentioned above, the timeframe to produce influenza vaccine typically takes about 6 months. With H1N1, Sanofi Pasteur was able to accelerate the timeframe which enabled delivery

of the first doses of vaccine only 4 months after the company received the seed virus from the CDC. This remarkable effort could not have been accomplished without our expertise and the dedication of our employees. Additionally our close coordination and collaborative work with FDA allowed Sanofi Pasteur to make vaccine in an accelerated fashion, while still ensuring vaccine safety and compliance with the legal and regulatory requirements of public health authorities. There has been a great deal of information and misinformation about vaccine delays and the reasons for such delays. (See Exhibit B for detailed timeline of Sanofi Pasteur pandemic actions.) Sanofi Pasteur began shipping H1N1 vaccine on September 29, 2009, which was earlier than forecast. As of November 13, 2009, Sanofi Pasteur has shipped 20 million doses and expects to ship several million more each week in November and December. We have orders for 75.3 million doses of bulk antigen for anticipated delivery between October and the end of December. Although we are still awaiting final direction from HHS on the formulation and fill of the final portion of these 75.3 million doses of bulk antigen, we are on track and fully anticipate we will be able to deliver all the 75.3 million doses as filled product by the end of December.

Notwithstanding that Sanofi Pasteur has largely succeeded in producing the H1N1 vaccine as initially projected, there were some factors that affected the delivery schedules for H1N1 vaccine, albeit only marginally.

- The production yield of this strain was initially significantly lower than standard. Lower yielding new strains are not unusual, even for seasonal flu vaccine; however, the initial yields for H1N1 were exceptionally low. Utilizing its expertise, the company was able to optimize the productivity of the seed virus such that yields are now approaching those traditionally seen for the annual seasonal vaccine. Going forward, we do not anticipate H1N1 yields to be a significant factor impacting future production schedules.

- By early August 2009, a series of clinical trials were initiated by both the NIH and Sanofi Pasteur in adult, elderly and pediatric populations. The initial data from these studies became available in early September. The first data came from NIH trials using H1N1 vaccine produced by Sanofi Pasteur. In part, this clinical information was necessary to finalize the language with CBER on the H1N1 vaccine packaging and the product insert. There was a delay of 2-3 weeks in obtaining final product labeling approval which was needed in order to complete product labeling and packaging. Initial supply projections were based on earlier receipt of this final labeling.
- Sanofi Pasteur originally anticipated that nearly all H1N1 vaccine orders would be for multi-dose vials. While the majority of orders are for multi-dose vials, a larger than expected number of single-dose and syringe presentations were also ordered, requiring some adjustments to filling and finishing schedules. To increase production throughput, Sanofi Pasteur worked with FDA to accelerate the approval of two new filling lines. In addition, the company identified and secured contract filling and packaging capacity to supplement its own internal resources. Throughout this process, the company has been in constant communication with HHS to discuss production and delivery schedule issues and has conducted 30 weekly telephone conferences with HHS agencies.
- The company faced an unprecedented and complex challenge of producing, testing, packaging, filling and distributing two influenza vaccines simultaneously.

In producing a complex biological product there is always an element of uncertainty regarding the production schedule. This is true regardless of the technology. In terms of bulk antigen production, the company is on schedule to deliver as per the original commitments made to HHS. As noted above, several unforeseen delays have contributed to an approximate 2-4

week delay in the delivery of finished and released vaccine in accordance with the order issued by HHS on August 21, 2009. These delays were communicated in early September to HHS, through our weekly phone calls, and delivery schedules were formally revisited and revised several times throughout September and October as new information became available. Even with the unforeseen delays, we are well-positioned, based on long standing experience in influenza vaccine production, to continue to fulfill our agreements with HHS. We are on track to make all 75 million H1N1 doses of vaccine available to HHS by the end of December. At the same time, Sanofi Pasteur stands firm on its original commitment to deliver all 50 million doses of seasonal vaccine to all customers who hold reservations. Seasonal distribution is expected to be completed by the end of November, which is still well ahead of the historical peak of seasonal influenza season.

VI. Sanofi Pasteur Vaccine Production Highlights (Exhibit B)

Specific timeline related to the production of H1N1 vaccine:

- On May 27, 2009, we received the A (H1N1) seed virus from the CDC which is an International WHO influenza reference center.
- Sanofi Pasteur began large-scale production of the vaccine on June 23, 2009.
- We began clinical trials of the vaccine in the US on August 6, 2009.
- The vaccine was licensed by the FDA on September 15, 2009.
- We began shipping vaccine to HHS on September 29, 2009 and shipments are ongoing as lots become available.
- We anticipate that we will be able to fill all 75.3 million doses of bulk antigen by the end of December, pending HHS orders for formulation and fill of the remaining bulk antigen.

VII. Vaccine Safety

In deciding to license the H1N1 vaccine, the FDA followed the same regulatory process by which it approves strain changes for the annual seasonal influenza vaccine. The H1N1 vaccine is produced by the same manufacturing process and in the same facilities used for seasonal vaccine.

Additionally, clinical trials were initiated and followed to evaluate the immunogenicity and safety of the vaccine. Data from several independent trials indicate that the H1N1 vaccine is similar in terms of immunogenicity and safety to seasonal influenza strains. The safety profile of the vaccine will be carefully and continually monitored in ongoing follow-up to the clinical trials for six months post immunization and by health officials as the public immunization campaign continues.

Conclusion

Sanofi Pasteur appreciates the opportunity to testify before the Subcommittees and to provide information on the vaccine production process for the 2009 H1N1 influenza vaccine. We are committed to working in partnership with the federal government and public health community to provide the American public with access to the H1N1 influenza vaccine as quickly as possible. We are confident that we are taking every step to produce a safe and effective product. I look forward to answering any questions.

sanofi pasteur
The vaccines division of sanofi-aventis Group

EXHIBIT A

H1N1 VACCINE DEVELOPMENT PROCESS

sanofi pasteur . Discovery Drive . Swiftwater, Pennsylvania 18370 . Tel.: 570-957-7187 . www.sanofipasteur.us
Sanofi Pasteur Inc.

sanofi pasteur
The vaccines division of sanofi-aventis Group

A (H1N1) Vaccine Production Process

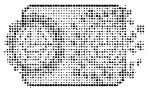
Surveillance

• Reference labs around the world collect wild virus carried by humans and characterize the genetic makeup. The virus is continually monitored and tracked by health authorities.

Strain Selection

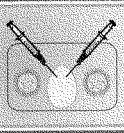
• World health officials anaylze and identify the dominant circulating strain.
• Health officals select virus strains and submit them to contracted laboratories to prepare seed virus.

• Laboratories distribute seed viruses to manufacturers to begin the production process.

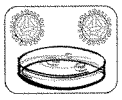


Preparation of Seed Virus

Seed virus is prepared by contracted laboratories using conventional reassortment or reverse genetics methods:
• Conventional reassortment - Two flu strains with the preferred features for a new vaccine are injected into an egg and the genes reassort naturally.



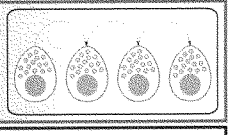
• Reverse genetics - Merges selected genetic information of the virus taken from the wild-type virus with the laboratory virus.



Seed Passaging and Selection

Once the seed virus is received, vaccine manufacturers begin passaging the seed virus in eggs to determine the optimum growth conditions and to improve virus yield by acclimating the virus to growing in eggs.

The working seed developed by the manufactuer is certified by the FDA.



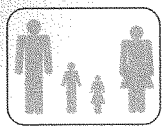
Bulk Manufacturing and Production[a,b]

• Millions of specially-prepared chicken eggs are used to produce the vaccine. Throughout the year, fertilized eggs are delivered to the manufacturer. Each egg is injected with the working seed.
• The eggs are incubated for several days to allow the virus to multiply. After incubation, the virus-loaded fluid is harvested.

Click here to see sanofi pasteur's Bulk Influenza Vaccine Manufacturing Process

Clinical Trials

• Portion of manufactured vaccine is used for clinical trials.
• Clinical trials may occur simultaneously with manufacturing.



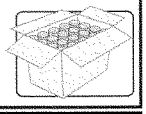
Purification and Testing[a,b]

• Manufacturers test the vaccine concentrate with specially prepared reagents provided by the FDA to determine the potency of the vaccine for immunization.

Formulation, Filling and Packaging

• Viral fragments from strains are collected from different batches, and combined upon completion of quality control tests.
• Upon FDA approval and licensing, the vaccine is released for distribution in time for immunization.

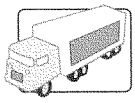
• Manufacturers begin filling the doses into vials and syringes, which are then sealed and carefully inspected before labels are applied to show the vaccine batch, lot numbers, and expiration date.
• Each lot must be specifically "released" by the FDA before manufacturers can ship supplies.



Shipping

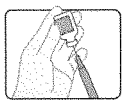
• Vaccine shipments take place over time as vaccine is produced.

• Health authorities determine distribution process.



Vaccination

• Health authorities will establish recommendations and priorities for vaccination.



[a]To ensure safety and purity, vaccine is produced in a clean environment where quality control experts enforce strict standards, continuously monitoring the process; [b]The majority of time for Bulk Manufacturing and Production and Purification and Testing is dedicated to testing and approval.

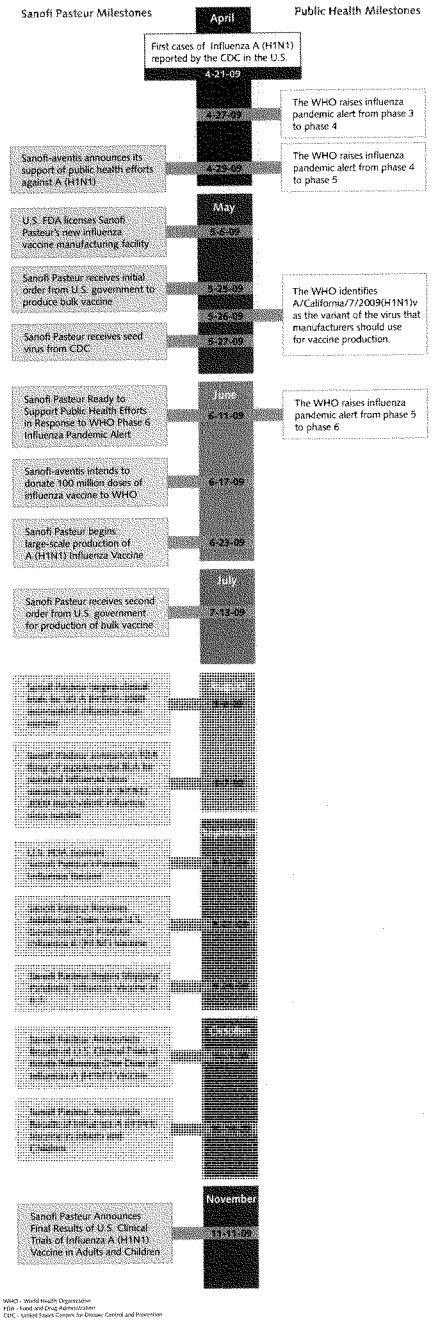
Courtesy of sanofi pasteur, May 2009

sanofi pasteur
The vaccines division of sanofi-aventis Group

EXHIBIT B

SANOFI PASTEUR PANDEMIC TIMELINE

Influenza A(H1N1) 2009 Timeline



Mr. STUPAK. Thank you.
Dr. Lakey.

TESTIMONY OF DAVID L. LAKEY

Dr. LAKEY. Chairman Stupak, Chairman Pallone, and Ranking Member Walden, my name is David Lakey. I'm the Commissioner of the Texas Department of Health Services, and it is an honor to be here today.

I've been in this position for 3 years and had the opportunity to serve in multiple public health events, including Hurricanes Dolly, Ike, and Gustav. My background is that I'm an infectious disease physician trained in both pediatric and adult infectious disease; and, like members that have testified earlier, I have been affected by this. I was the first State health officer to be infected, and my family was also infected.

History has taught us that pandemics occur. The challenges, the timing, and severity of the next pandemic, with the last one being 40 years ago, State and Federal governments have planned and exercised their plans over many years.

The challenge in 2009 was that this pandemic was significantly different than the high-severity pandemic that many of us had planned for. And it also occurred in our continent and, therefore, we were having to respond as we were also figuring out this disease and defining the severity.

Because of these differences, our State and Nation as a whole had to rapidly flex our plans to match this situation. This ability to adjust your plans according to what you see is a critical component to any successful response. This flexing of our plans included modifying our plans related to the distribution of the novel H1N1 vaccine.

Previous pandemic plans had anticipated a high-level, high-severity pandemic; and many of those had focused on mass vaccination clinics. However, mass vaccination clinics have many challenges, as I have listed in the information that I have given you.

We have also looked at school-based clinics; and they have their own challenges, like I've listed in the information that I have provided. And so both of those strategies have significant challenges.

In light of our real-world experience, Texas and many other States decided that we needed to adjust these plans related to the severity of this pandemic. We decided to use the private sector and the public health providers, the local health departments, the SUHCs that are in our State as much as possible to direct to provide the vaccine to the patients that they usually care for. This method allows us to target the vaccine to those priority populations. We've also worked with pharmacies to figure out how we can provide vaccines to pharmacies so they can provide it in that private sector.

Now, different States are using alternative strategies based on their experience, their public health infrastructure. Public health is structured in many different ways across the United States in the resources and the capabilities that each State had.

In order to facilitate this, Texas had to develop new resources, new tools in order for us to register providers and to pre-identify individuals within each priority population; and we made that

Web-based application and linked it to our primary flu information source at www.TexasFlu.org.

Currently, we have 12,600 health care providers in Texas that are part of this distribution system. They have registered to receive vaccine. And, of those, we have been able to apportion vaccine to 7,000 providers in our State. In order to complement the system, we have worked with 211 in order to address concerns from health care providers or from the general public in order to steer them to where we can find vaccine.

Due to the limited supply that has been discussed today, States have had to further adjust these plans to help ensure the most vulnerable individuals are protected. For example, Texas so far has been allocated 3.7 million doses. Of that, we've been able to order 3.3 million doses. However, that's the amount of vaccine that we were told that we would have available back a month ago in mid-October. Because of the limited supplies, we've had to target our populations based on risk and the type of vaccine that was available and then gradually expand those groups as additional vaccine became available to us.

I've outlined the system for the distribution of vaccine to providers in the State of Texas in the information that I've provided you.

I note that once the FDA approves and releases a lot the CDC informs the States about the amount and the type of vaccine that is available and then a lot of additional work has to take place. We have to match the providers that we know that want vaccine with the vaccine that is available, ensure that they still want that vaccine, and make sure that they're ready to accept that vaccine. It is a challenge to match the current priority groups and to the providers that these populations serve, and we also have to ensure that we have good geographic distribution across a large State like Texas. This can be a complicated and a tedious process.

We have been adjusting our plans as we have gone through this event and recently adjusted our plans to ensure that 20 percent of all the allocation that came to our State went to the local health department so they could fill in the gaps that that private provider base was not supplying.

I would like to finish my time by mentioning several of the challenges that we in State public health have faced as part of this pandemic.

Note this pandemic only occurred 7 months ago; and, as has been noted here, a lot of work has taken place across the United States in that relatively short amount of time. Furthermore, all this work was accomplished in a background of significant reductions in public health across the United States. We estimate approximately 15,000 public health positions have been eliminated over the last year across the United States.

Now, despite the success, there is a national perception that we are falling short, partly because I believe we set expectations too high about the amount of vaccine that would be available initially and the national supply hasn't been adequate to meet the public demand that was created. Additionally, we created the perception that vaccine would be available to all priority groups immediately. These priority groups account for almost half of the U.S. popu-

lation, and because of the supply limitations we as a State then had to narrow down those priority groups in order to get the best use of that limited resource.

There's also confusion about that process of how vaccines are allocated, ordered, and shipped and the steps that go in to ensuring it gets to the individuals that need it. And there's differences between how the States manage that because of the different structures within public health and their State. These misperceptions have led to false impressions that States are either not pulling down their full allotment or, second, that they're not being allotted the amount that should be according to their population. And both of those impressions are false.

There is also a challenge in developing tools to link individuals that are seeking vaccine with the providers that have the vaccine. Various tools have been developed, including Web-based tools, but there's challenges with those tools. That the providers that we're shipping doses to may only receive a small amount of vaccine. If we put their name on a Web page we may steer a lot of individuals to those sites and give another false impression that vaccine would be available, and I think that would compound the current challenges that we are having.

Instead of doing that, we in the State of Texas have worked with 211 and provided them a list of the providers and have steered individuals to 211; and then we can give individual guidance on where they can seek a vaccine in their community. And we've also, as I noted earlier, sent additional vaccine to the local health providers.

Mr. STUPAK. Please summarize.

Dr. LAKEY. OK. I think we also have a challenge related to the public health that has been funded, and that's been alluded to earlier today, the intermittent nature in which some of the funds have come down, one-time funding, and that has been difficult.

But I would like to say thank you for the funds that have been made available to the public health emergency response funds this last year. Those have been very important.

And, finally, I would like to say that we really appreciate the commitment of the CDC and the Office of the Assistant Secretary for Preparedness and Response for how they've engaged local and State public health. We have continuous dialogue with them in order to work out issues and figure out how we can best serve the population of the United States.

Thank you.

[The prepared statement of Dr. Lakey follows:]

Testimony before the Committee on Energy and Commerce
U.S. House of Representatives
David L. Lakey, M.D., Commissioner
Texas Department of State Health Services
November 18, 2009

Introduction

Good morning, my name is David Lakey, Commissioner of the Texas Department of State Health Services. I am a pediatric and adult infectious disease physician, and have served as commissioner for approximately three years. During my tenure as commissioner, I have led the Texas public health response to multiple events including Hurricanes Dolly, Gustav and Ike.

History has taught us that pandemics occur periodically. However, the timing and severity of the next one was unknown. The last pandemic was 40 years ago. Federal and state governments have planned and exercised for an influenza pandemic for many years.

The 2009 pandemic is significantly different from the high severity "bird flu" pandemic for which our nation had been preparing. Because this pandemic began on our continent instead of overseas, we had a shorter time to initiate response efforts. We had to define the illness and the severity as we responded. The

fortunate news throughout this event is that, although this virus spreads easily, its severity is at the lower end of the scale.

Adjusting Vaccine Distribution Strategies

Because of these differences, our state and the nation as a whole had to rapidly flex plans to match the situation. The ability to adjust plans is a critical component to any successful response. For this pandemic, this included modifying plans to distribute the new H1N1 vaccine.

Previous pandemic plans, due to the anticipated high level of severity, had focused on mass vaccination clinics. However, mass vaccination clinics have specific challenges. These challenges include: insufficient supplies for the anticipated demand, long lines, the inability to vaccinate all who show up to be vaccinated, exposure of high risk individuals, and logistical issues, such as record-keeping and pre-registration to receive the vaccine. Mass vaccination is resource intensive and may divert health care resources away from taking care of patients.

School-based clinics are a means to vaccinate the masses. Challenges with these clinics include obtaining informed consent

and the difficulty targeting the highest priority patients when vaccine is scarce.

In light of our real world experience with this pandemic, Texas and many other states decided to adjust these plans and strategies.

We decided to use the private sector and public providers as much as possible to provide the vaccine directly to their usual patients. This includes the use of pharmacies as vaccination locations. This method allows providers to pre-identify their priority populations, thus allowing individuals to obtain the H1N1 vaccine the same way they obtain their usual health care and seasonal flu shot. This method allows a more targeted approach in reaching priority populations.

Different states are using alternative strategies based on their experience, public health structure, resources and capabilities. Some states, like California, are utilizing larger vaccination clinics, while others, like Texas and Massachusetts, are relying heavily on the private sector to distribute vaccines.

To accommodate the delivery of vaccine to health care providers across Texas, we developed a new tool to allow providers to register efficiently to be part of this strategy and to pre-identify the number of individuals they intend to serve in each priority population. This web-based application is linked to our primary flu information source, www.TexasFlu.org.

Currently, ~12,600 health care providers in Texas have registered to receive the vaccine, and, of these, vaccine has been apportioned to more than 7,000.

To complement the registration process and to address concerns and questions from health care providers and the public about the many facets of the H1N1 pandemic, our department has contracted with Texas 2-1-1, a program that serves as the single point of coordination for statewide health and human services information and referral in Texas.

Supply

The amount of vaccine available to all states is obviously much less than was predicted. Thus, states have had to further adjust their plans to help ensure the most vulnerable are protected.

Texas continues to order the state's full allocation of the H1N1 vaccine as quickly as possible, with more than 3 million doses ordered and 3.3 million doses allocated as of November 13. Note, however, that this amount of vaccine was originally predicted to be available to Texas by mid-October.

Because of this limited supply, states have to target populations based on risk and type of vaccine that is available. This will gradually expand to additional groups as the supply and the type of vaccine available increases.

For example, only the nasal spray type of the vaccine was available to Texas initially. The nasal form of the vaccine cannot be used with pregnant women or individuals with chronic conditions. For this reason, we had to focus our distribution on providers that cared for young children 2-4 years of age with no underlying health conditions and the health care providers without high risk conditions that serve that population.

As additional vaccine has become available, we have been able to reach other groups. We are now able to vaccinate pregnant women, people who live with or provide care for infants younger

than 6 months, children 6 months – 4 years of age, high risk children 5 - 18 years of age, and health care and emergency medical services personnel with direct patient contact including EMS. We have just begun allocating vaccine for high risk adults. However, we have not received the necessary volume of vaccine to reach the population of healthy children.

Distributing vaccine to the providers

Once the FDA approves and releases vaccine lots, that vaccine becomes available for distribution to the states. Almost daily, CDC informs states the amount and type of vaccine that is available to be ordered. We then determine where this vaccine should be shipped and confirm that the providers still want the vaccine.

It is a challenge to match the current priority groups with the providers that serve these populations in a way that considers the vaccine types and also ensures good geographic distribution. This can be a complicated and tedious process.

Texas apportions available vaccine to health care providers serving the highest priority population. We recently adjusted

our plan by allocating 20 percent of all vaccine to local health departments to fill identified gaps found at the local level.

Once Texas places an order, McKesson, the national distributor, ships large vaccine orders directly to providers and bulk vaccine to GIV, Texas' contracted third party distributor. This contractor assists the state in getting vaccine to smaller providers across the state.

Challenges

I would like to finish by mentioning several of the challenges we in state public health face as part of this pandemic that began only seven months ago.

a. During this time, we as a nation have identified and characterized this disease, isolated the virus, figured out how to best grow it in the lab, converted vaccine manufacturing plants over to H1N1 production, performed clinical trials, and developed new vaccine allocation and distribution systems. This is an incredible amount of work over this short time period.
b. All of this work was accomplished in light of significant reductions to public health resources across the nation

and the loss of the public health workforce in the economic downturn. We estimate that over the last year 15,000 public health jobs have been lost nationally.

c. Despite our success, there is a national perception that we are falling short, partly because we set expectations too high about the amount of vaccine that would be available initially.
    - The national supply hasn't been adequate to meet the public demand that was created.
d. Additionally, we created the perception that vaccine would be available to all priority groups immediately. These priority groups account for over half of the U.S. population.
    - Because of the supply limitations, states have had to narrow these groups and focus on those most severely impacted by the disease.
e. There is also confusion about when vaccines are allocated, ordered, shipped and the steps that go into getting vaccine to the people that need it. Some of the misperceptions relate to differences in how states manage vaccine distribution. These misperceptions have led to false impressions that either states are not being allocated

their entire allotment, or that states are not ordering their allotment timely. Both impressions are false.

f. There is a challenge in developing tools to link individuals seeking vaccine with those providers that have it. This is complicated by the limited supply.
   - Various tools have been developed, including web-based systems.
   - The challenge is that most of the providers we are using are being shipped a limited number of doses based on their priority populations. They do not have sufficient supplies to expand out of these groups. Publicizing all these provider names on a web-based system could cause another misperception that vaccine would be available to the general population at these sites. This would quickly overburden these health care providers. The result is that these providers may not participate the next time we call for their assistance.
   - In Texas, we have attempted to address this challenge by:
     1. Using 2-1-1 to link individuals to providers.

2. Providing vaccine to local health providers to serve as a safety net if their usual provider does not have vaccine.

- We are in the process of implementing a flu locator now that vaccine is becoming more available across provider groups. This locator will target public health care providers and larger providers, such as pharmacies.

g. We have a challenge with the intermittent nature in which pandemic and disaster preparedness has been funded in the past.

- We appreciate the federal government's response to the 2009 H1N1 pandemic and the help Texas and the other states have received, including the Public Health Emergency Response (PHER) funding and the provision of vaccines.
- However, previous one-time pandemic planning funding did not allow us to sustain the resources needed for a response like we are currently undertaking.
- This will not be the last pandemic to be seen in our lifetime.

- To continue to be better prepared for public health threats and to protect our individual states and the nation, it will take a continuous and sustained investment.

Finally, we appreciate the commitment of the CDC, the Office of the Assistant Secretary for Preparedness and Response, and other federal agencies that have worked closely with state and local public health. We are in continuous contact and talk on the phone multiple times a week working to find solutions to these difficult issues. Our ultimate goal is to protect the health, safety and well-being of our citizens.

Thank you.

Mr. STUPAK. Thank you Doctor.
Dr. Levi, your testimony.

TESTIMONY OF JEFFREY LEVI

Dr. LEVI. Thank you Chairman Stupak, Chairman Pallone, and Ranking Members Walden and Mr. Green. Thank you for this opportunity to speak to you today about our preparation and response to the 2009 H1N1 pandemic. I'm here on behalf of Trust for America's Health, a nonprofit, nonpartisan advocacy organization dedicated to saving lives by making disease prevention a national priority.

While I understand that today's hearing is a result of considerable frustration with the current H1N1 vaccination program, I wanted to emphasize four critical points:

First, the public health system at all levels of government has moved with remarkable speed in approving an H1N1 vaccine and getting vaccines to as many Americans as supply has permitted. We've moved as fast as or faster than any other country in the world.

Second, the vaccine is well matched to the circulating virus. It has been proven to be safe and effective in clinical trials and offers the best possible protection against the disease.

Third, whatever our concerns with production capacity are today, had the Federal Government not made the multi-billion dollar investments in enhanced vaccine production capacity since 2005 we would be in far worse shape. The limits on supply we are experiencing are the limits imposed by the science and technology. The decision to use a central purchasing and distribution approach has assured that as supply has become available it has been equitably distributed across the Nation.

And, finally, the Federal Government has been remarkably transparent with the American people about this pandemic since it began last spring. Public health officials have leveled with the American people, making appropriate adjustments and recommendations as our understanding of the nature of the pandemic has evolved and as supply issues have arisen.

The response to this pandemic has mobilized all levels of government. While the Federal Government has assumed responsibility for distributing vaccines to State and local health departments, each locality is then responsible for developing its own policies and systems for administration of the vaccine. This has posed a number of challenges, particularly in a context of vaccine shortages.

First, local health officials received constantly shifting information about how much vaccine would be available and when. This is clearly an issue that has not only created confusion among the American people, it has also made the job of local health officials far more difficult.

Second, the largest mass vaccination campaign in U.S. History is taking place when State and local health departments are experiencing devastating losses because of the recession. While the Federal Government has rapidly pumped almost $1.5 billion into State and local health departments for pandemic response, this does not address the underlying decline in the core capacity of health departments.

And, third, public confusion may well have been exacerbated by the fact that each State and locality has determined how to distribute its supply once received from the Federal Government. Although each health department based their plans on a larger supply of vaccine, HHS may want to revisit this issue and consider some standardization in future emergencies.

It is our hope that this hearing will contribute to the public's understanding of the complexities of the current pandemic influenza vaccine campaign. Among the key initiatives TFAH maintains are critical to the success of the response to this and future epidemics are, first, an education campaign is needed to assure the American people about the safety and effectiveness of influenza vaccines and all vaccines in general. It is important to remind Americans that even with the delays in vaccine availability they should get vaccinated as soon as they can. We have not seen the end of this pandemic.

FDA should move forward in assessing new technologies that are already in use in other countries, including the use of adjuvants and cell-based vaccines. However, to have moved forward on an expedited basis without the standardized review would probably have undermined an already fragile confidence in the vaccine system.

Congress and the administration should also come to a consensus on what is an appropriate level of investment in new technologies. This pandemic has demonstrated the Nation still has a long way to go, not just in vaccine technology but with regard to diagnostics and antiviral treatments as well as personal protection equipment. The Biological Advance Research and Development Agency has been chronically underfunded since its inception. Its support is critical to moving promising developmental technologies into mass production. Professional estimates suggest that BARDA needs an annual appropriation of $1.7 billion, rather than the current $275 million to achieve its mission.

We need to provide ongoing support to State and local health departments in building capacity to respond to public health emergencies. Just as we don't fund fire departments at the moment the fire breaks out, we must move away from emergency funding mechanisms to respond to public health emergencies. This is one reason TFAH supports the mandatory funding for core public health functions that is part of the House health reform bill.

Finally, Congress and the administration should assure replenishment of the Strategic National Stockpile for supplies that have been distributed to States such as N95 respirators, surgical masks, and antivirals. We do not know what demand the future wave of this pandemic strain will require of the SNS, nor can we forget the potential for other pandemic strains emerging, such as the H5N1 bird flu that was a primary concern until last spring.

This pandemic has shown our government at its best and highlighted many of the ongoing weaknesses in our public health system. As we continue to ramp up our response to this pandemic, we must also take steps necessary to assure that when the next public health crisis occurs a stronger system is in place and capable of responding quickly, effectively, and nimbly.

Thank you, and I look forward to your questions.

[The prepared statement of Mr. Levi follows:]

House Committee on Energy & Commerce
Joint Hearing on H1N1 Preparedness: An Overview of Vaccine Production and Distribution
Testimony of Jeffrey Levi, PhD
Executive Director, Trust for America's Health
November 18, 2009

Chairmen Stupak and Pallone, Ranking Members Walden and Deal, and members of the subcommittees: Thank you for the opportunity to speak with you today on issues related to the preparation and response to the 2009 H1N1 novel influenza A pandemic. I am here on behalf of Trust for America's Health (TFAH), a nonprofit, nonpartisan advocacy organization dedicated to saving lives by making disease prevention a national priority. For the past five years, TFAH has advocated for increased investments in preparedness and response to a potential influenza pandemic. We have published numerous reports focused on these issues, including two related to the current H1N1 pandemic.

While I understand that today's hearing is a result of considerable frustration with the current H1N1 vaccination program, I want to emphasize four critical points:

- The public health system at all levels of government has moved with remarkable speed in getting vaccines to as many Americans as supply has permitted. We have moved as fast as or faster than any other country in the world. The United Kingdom, for example, just began its vaccination campaign in late October -- even though there is more vaccine production capacity in the U.K. than in the U.S. Similarly, the French vaccination campaign did not begin until last week
- The vaccine is well matched to the circulating virus. It is proven to be safe and effective in clinical trials. The H1N1 vaccine offers the best protection against the disease available to the American public.
- Whatever our concerns with production capacity are today, had the federal government not made the multi-billion dollar investment in enhanced vaccine production capacity since 2005, we would be in far worse shape. The limits on supply we are experiencing today are the limits imposed by the science and technology. We are depending on an inherently unpredictable technology and we are, unfortunately, still a few years away from U.S. approval of newer, more reliable technology.
- The federal government has been remarkably transparent with the American people about this pandemic since it began last spring. The federal effort appears to be well coordinated with all cabinet and subcabinet officials working from the same playbook. Public health officials have leveled with the American people -- making appropriate adjustments in recommendations as our understanding of the

nature of the pandemic has evolved. The same has held true as supply issues have arisen. While I cannot speak to when senior Administration officials should have known about serious supply problems, when they did become aware of them, they adjusted policy and messaging appropriately. This has led to some understandable confusion among the public, but it has reflected an honest attempt to reflect the current state of knowledge.

Current production capacity reflects the pay-off of a multi-year investment.

While there is understandable dissatisfaction with the current vaccine production levels, it is important to note that if this pandemic had hit in 2005, getting a vaccine to the American public within six months would likely have been nearly impossible. In 2005, only two manufacturers were licensed to produce influenza vaccine in the U.S.[1] The Department of Health and Human Services' (HHS) Pandemic Preparedness Plan, issued in November 2005, called for increasing domestic pandemic vaccine manufacturing capacity to inoculate 300 million persons within six months of the onset of an outbreak.[2] Government officials estimated that this capacity would take approximately five years to ramp up. According to a 2008 Congressional Budget Office (CBO) analysis, the maximum capacity for a 2006-2007 pandemic flu vaccine would have been 120 million doses (of which 50 million would have been produced domestically).[3]

Today, the Centers for Disease Control and Prevention (CDC) and HHS estimate there will be enough vaccine for every American, between domestic and foreign production. The near-term availability of sufficient pandemic vaccine, albeit slower than hoped for initially, is due to an investment that began in FY 2006, when Congress approved $3.2 billion for advanced development, infrastructure building, and purchase of vaccines.[4] The federal government invested in retrofitting and expanding capacity in vaccine manufacturers that had domestic production facilities -- MedImmune and sanofi Pasteur -- and ensuring a year-round supply of eggs.[5] HHS also developed contracts with foreign-based facilities to develop vaccine for the U.S. market. By mid-September 2009, the U.S. Food and Drug Administration (FDA) had approved four companies to produce H1N1 vaccine for the U.S.,[6] earlier than any European country, and a fifth, GlaxoSmithKline, was licensed by the FDA last week,. Six companies have also received advance development contracts for building U.S. cell-based vaccine production facilities, and the

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[1] *A Killer Flu?* Trust for America's Health, June 2006. p. 10. Available from: http://healthyamericans.org/reports/flu/Flu2005.pdf

[2] BARDA Influenza and Emerging Disease Program. Available from: https://www.medicalcountermeasures.gov/BARDA/MCM/panflu/panflu.aspx.

[3] Congressional Budget Office, U.S. Policy Regarding Pandemic-Influenza Vaccines, Sept. 2008. Available from: http://www.cbo.gov/ftpdocs/95xx/doc9573/Frontmatter.1.2.shtml.

[4] DHHS, Report to Congress: Pandemic Influenza Preparedness Spending, January 2009. Available from: https://www.medicalcountermeasures.gov/BARDA/documents/hhspanflu-spending-0901.pdf

[5] CBO, 2008.

[6] U.S. FDA, "Influenza A (H1N1) 2009 Monovalent." Available from: http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm181950.htm.

most successful companies should receive additional contracts to bring production online.[7]

New technologies for vaccine production are not yet FDA-approved. Use of technologies that might be perceived as "experimental" could undermine public confidence in a pandemic vaccine.

There has been some debate about whether the United States could have used emergency authorities held by the FDA to permit different vaccine technologies to be used during this pandemic campaign so as to speed production and/or increase the amount of vaccine available. To date, the FDA has not approved cell-based vaccines, a technology whose development the U.S. government is supporting and is the basis for production of some pandemic (and seasonal) vaccine in Europe. Cell-based vaccine is more stable and allows for a faster production process. Similarly, some countries are using vaccine that contains an adjuvant -- a chemical additive that permits use of smaller doses of the actual vaccine thus dramatically extending the supply. While swift assessment of these technologies by U.S. officials is certainly called for, use of these technologies during the current pandemic would have been unwise. Given the very high level of skepticism in the U.S. (and around the world) about vaccines in general and some of the concerns about the pandemic vaccine in particular, it has been critical for federal officials to reassure the public that this is the very same vaccine manufacturing process that hundreds of millions of Americans have taken safely to protect themselves against seasonal flu. Clinical trials for this pandemic vaccine were thorough and efficient, providing additional reassurance to the American people. Approval of cell-based vaccines against a novel influenza virus, when not currently approved for the seasonal virus, would have been considered experimental by many Americans. There may have been a misperception that the vaccine had not gone through the usual rigorous FDA approval process. This would have complicated efforts to encourage all Americans, especially those at highest risk, to receive a vaccination against the H1N1 virus.

With respect to the use of adjuvanted vaccine, which is currently not approved by the FDA for seasonal or pandemic flu, those nations using it have found it to be controversial due to public perceptions. In Germany, for example, there have been protests because government officials were given a non-adjuvanted vaccine, while the public is receiving an adjuvanted vaccine. Some German professional medical societies are now recommending against the use of an adjuvanted vaccine for anyone.

The government has moved as rapidly as possible to move vaccine from production lines to vaccine clinics. Using a centralized distribution system has assured equitable geographic distribution of a limited supply.

As vaccine supplies have become available, the federal government has assured that vaccines have moved as quickly as possible to local vaccination sites. The government could have waited until a sufficient amount of vaccine was on hand before beginning to distribute it to immunization sites. This *may* have reduced some of the confusion we

[7] CBO, 2008.

have experienced as delivery expectations were repeatedly revised downward. But this would have resulted in delaying the protection of millions who are at risk.

The policy decision that the federal government should be the central purchaser and distributer of vaccine was wise from public health and ethical standpoints. Centralization has permitted the federal government to control the flow of the limited supply. Every state is receiving vaccine on a per capita basis, rather than based on private ordering, state budgets, population demographics, or political decision-making. An influenza outbreak does not acknowledge or respect state borders, and no American should be less protected based on where he/she lives. If the federal government had depended on a private distribution system, as the previous Administration had suggested, we likely would have seen a repeat of the 2004-2005 seasonal flu vaccine shortage scenario -- wherein some providers would have sufficient vaccine, while others would have little or none, depending entirely on which vaccine manufacturer had been contracted with to supply vaccine. Although all states are temporarily experiencing shortages, all states are suffering shortfalls equally. The situation is not always as clear on the local level, where distribution within states appears uneven in some cases.

This is not to say that there have not been glitches in this new, untested, centralized system. But as best TFAH can determine, federal health officials have moved as rapidly as possible to address the problems.

Supply shortages, the recession, and a decentralized approach to administration of vaccines in each local community contributed to varying capacity at the local level and confusion among the public.

While the federal government has assumed centralized responsibility for vaccine distribution to state and local health departments, each locality is then responsible for developing its own policies and systems for administration of vaccine as it becomes available. This has posed a number of important challenges, particularly in a context of changing messaging resulting from shortages of both seasonal and H1N1 vaccines:

- First, local officials received constantly shifting information about how much vaccine would be available and when. This makes setting parameters for vaccine administration very difficult. It is nearly impossible to know why the communications breakdown between federal officials and industry occurred with regard to the pace of production. But this is clearly an issue that has not only created confusion among the American people; it has also made the job of local health officials far more difficult in an already challenging situation.
- Second, the largest mass vaccination campaign in U.S. history is taking place during an economic recession and when state and local health departments are experiencing devastating losses. According to a survey by National Association of County and City Health Officials (NACCHO), 15,000 positions have been lost in local health departments since the beginning of 2008. While the federal government has rapidly pumped almost $1.5 billion to state and local health departments for pandemic response, this does not address the underlying decline

in the core capacity of health departments. We are seeing the result of decades of under-investment in public health capacity. It cannot be rebuilt on an emergency basis.

- Third, public confusion may well have been exacerbated by the fact that each state and locality has determined how to distribute its supply once received from the federal government. While all jurisdictions have kept to the general prioritization of certain populations, they have often acted differently in terms of which individuals within the prioritized grouping would get vaccine first. This may well have been due to how supply was ordered by the states and/or distributed within the states. For example, some localities have prioritized health care workers, some have prioritized the vaccination of children, and still others have made pregnant women a top priority. Population demographics differ from state-to-state, so it is sensible to allow some flexibility between locales (for example, if the pandemic had targeted seniors, Arizona and Florida may have very different distribution plans than other states). However, the wide variation in distribution methodologies has created a fair amount of confusion among the public. Although each health department based their plans on a larger supply of vaccines, HHS may want to revisit this issue and consider some standardization in future emergencies since it is not unreasonable for the American people to expect some level of consistency in approach. Otherwise, they may think that the target population hierarchies articulated by the federal government are not science-based.

Near-term and long-term next steps:

It is our hope that this hearing will contribute to the public's understanding of the complexities of the current pandemic influenza vaccine campaign. Among the key initiatives TFAH maintains are critical to the success of the response to this and future pandemics are:

- An education campaign is needed to assure the American people about the safety and effectiveness of this (and other) influenza vaccines and all vaccines in general. It is important to remind Americans that even with the delays in vaccine availability, they should get vaccinated as soon as they can. It is not clear that the pandemic has peaked, and even if it has, many who might yet get sick are still at risk and could be protected by a vaccine. Moreover, historically there is always the danger of a third pandemic wave, which may or may not be more severe than the previous two waves. So being vaccinated now will be critical protection for those who have not become ill during the initial waves.
- FDA should move forward in assessing new technologies that are already in use in influenza vaccines in other countries -- including use of adjuvants and cell-based vaccines. If data from other countries do not meet FDA's standards, FDA should work closely with industry and the National Institutes of Health (NIH) to collect the data needed for decision making.
- Congress and the Administration should come to a consensus on what is an appropriate level of investment in new technologies. This pandemic has

demonstrated that the nation still has a long way to go, not just in vaccine technology, but with regard to diagnostics and antiviral treatments as well as personal protection equipment for those exposed to influenza in the workplace. The Biological Advanced Research and Development Agency (BARDA) has been chronically underfunded since its inception. Its support is critical to moving promising developmental technologies into mass production. Professional estimates suggest BARDA needs an annual appropriation of $1.7 billion, rather than the current $275 million, to achieve its mission.

- We need to provide ongoing support to state and local health departments in building capacity to respond to pandemics and other public health emergencies. As discussed previously, this emergency has occurred at a time of state and local level budget crises, with associated reductions in the public health workforce. Federal support for preparedness has been inconsistent at best. Until the emergency funds provided this summer to state and local health departments, no funds for pandemic preparedness had been appropriated since FY 2006. Underlying preparedness funding has been declining over the last several years as well, down 27 percent since FY 2005 in inflation adjusted dollars. Congress must assure a consistent level of preparedness capacity at state and local health departments on an ongoing basis. Just as we don't fund fire departments at the moment a fire breaks out, we must move away from the emergency funding mechanisms to respond to public health emergencies. This is one reason TFAH supports the mandatory funding for core public health functions that is part of the House health reform bill.
- Congress and the Administration must also address several other critical aspects of pandemic response capacity. These include:
    - Replenishment of the Strategic National Stockpile (SNS) for supplies that have been distributed to the states. This includes N-95 respirators, surgical masks, and antivirals. To our knowledge, to date only the depleted supply of pediatric formulation of Tamiflu has been ordered for restocking. We do not know what demand a future wave of this pandemic strain will require of the SNS; nor can we forget the potential for other pandemic strains emerging -- such as the H5N1 bird flu that was of primary concern until last spring.
    - Heretofore, most health system preparedness funding has been focused on a hospital-based response, whereas in this pandemic, we have seen significant overload in the ambulatory care system. We need to examine the impact this pandemic has had on hospital and ambulatory care systems and reassess whether our preparedness plans have provided an appropriate level of support to *all* aspects of the health care system.

Conclusion

The 2009 H1N1 influenza pandemic has both shown our government at its best and highlighted many of the ongoing weaknesses in our public health system. As we continue to ramp up our response to this pandemic -- and provide the protection the American people rightfully expect their government to make available -- we must also

take the steps necessary to assure that when the next public health crisis occurs, a stronger system is in place and capable of responding quickly, effectively, and nimbly.

Mr. STUPAK. Thank you, and thank you all for your testimony.

Dr. Narasimham, how do you say your last name?

Dr. NARASIMHAM. Narasimham.

Mr. STUPAK. Narasimham. Let me ask you about November 3rd. You signed a letter back to us, to the committee. We asked a number of questions of all the companies—the four or (c) companies here, and one that had caught my eye was found on page 3, point number 5.

You said, while the government ordered bulk doses of our proprietary adjuvant MF59 which enhances the potency of the flu vaccine, it, based on recently available data, could have quadrupled the number of doses supplied. The government ultimately determined that the use of adjuvant was not warranted to combat the pandemic and elected not to license or use the emergency use authorization.

These are a number of the questions I asked the previous panel:

It's my understanding—and correct me if I'm wrong—do other countries use your MF59 doses with the adjuvant in it?

Dr. NARASIMHAM. That's correct. We have two H1N1 vaccines licensed in Europe and in other parts of the world with MF59, and we're exclusively providing adjuvanted vaccines outside the United States.

Mr. STUPAK. Is there a safety issue with that? I think the FDA said they had not approved it. And if my memory serves me correctly you've been trying to get this approved in the U.S. since 2007.

Dr. NARASIMHAM. The MF59 is not approved in the U.S., but we have licensed it in Europe in 1997. We have a pretty broad range of clinical studies now, up to 200,000 subjects in noncontrolled trials and about 40,000 subjects in controlled clinical studies. To date, we have not seen any significant safety signal, so we've continued to provide that data to FDA on an ongoing basis.

Mr. STUPAK. In my 15 years here, I have always been on drug companies to make sure these things are safe. You said it's been licensed since 1997 in the rest of the world?

Dr. NARASIMHAM. That's correct, in the elderly. And for the H1N1 now we have it licensed down to 6 months of age. So for the H1N1 the adjuvanted vaccines overseas are licensed from 6 months through the elderly.

Mr. STUPAK. I thought I heard Dr. Goodman on the last panel indicate that they've ordered a stockpile of this MF59 from your company.

Dr. NARASIMHAM. That is correct. We are maintaining a stockpile in Louisville, Kentucky.

Mr. STUPAK. And I asked him, then when were they going to use it? When do we get to the point, whether it's adjuvanted or not, we're going to use it? Because the pandemic is so great here in the United States. Have they ever discussed that with you?

Dr. NARASIMHAM. We had a discussion with them in early May as to how to proceed. And the decision at that point was to only use licensed platforms, U.S.-licensed platforms moving forward. Through the summer and into September, we've maintained the capability to always use the adjuvant in case the data suggested that was needed. We continue to stand ready to do that, but to date—

and we also have prepared the EUA application in collaboration with HHS. We have not been asked to date to move forward with that.

Mr. STUPAK. I think in your testimony you said that you started discussing this in 2007—whether you should use adjuvant or not with the FDA in 2007. You applied for a license in 2008, is that correct?

Dr. NARASIMHAM. We applied for a new drug application, an IND, an investigational new drug, in 2008; and we've been going back and forth with the FDA since then.

Mr. STUPAK. Do you see this—the adjuvant issue, that just won't be with H1N1 but really any kind of a vaccine. Is that because you can quadruple it, at least in this case at least quadruple your doses?

Dr. NARASIMHAM. That's correct. There are a number of benefits from the adjuvant.

One is you improve the immunogenicity so that if you have children or the elderly who do not respond you can actually make them respond to the vaccine. You can increase the number of doses.

Another valuable thing of the adjuvant, which was not as relevant in this case, is if the virus changes—so in the spring, if the virus changes, there might be the need to revaccinate everyone in the U.S. Whereas with the adjuvant you can cover a certain amount of variation in the virus we've seen in our clinical studies. Now, we haven't looked at that yet in this case, but it would at least provide you that flexibility.

Mr. STUPAK. Dr. Levi, is it fair to ask you—is it fair to say that this is something we ought to look at as a country? I mean, the FDA hasn't licensed it. I know you mentioned in your testimony about making sure drugs are safe and approved, and that's my concern and I'm sure everyone's concern on this panel. Are we missing something here? Is there something we should look at closer?

Dr. LEVI. It's definitely something we should look at closely. I believe the FDA is doing this in a good-faith manner. I think when you think about who we are targeting for this vaccine, the bulk of the data for using the adjuvanted vaccine occurs with the elderly. That's not who's targeted in this vaccine, and so we're just beginning to get the kind of data that would be associated with kids.

But I think the larger question is we have so much vaccine hesitancy in this country, so much inaccurate knowledge about whether vaccines are safe and particularly whether this flu vaccine is safe, to add on through an emergency use application a new element that may indeed be safe could well have undermined the efficacy of this campaign.

Mr. STUPAK. So this one has been around for, as I have said, I think 1997 or so and then approved. Would it be prudent to maybe leave the decision to the parent whether or not they wanted their child to be vaccinated with an H1N1 vaccine that's juvenated as opposed to not.

Dr. LEVI. It is sometimes hard to understand why there is so much hesitancy around vaccines in general and this particular vaccine. I think we had a real public health question as to whether people would accept a vaccine that had a new product in it.

Now, if things had been worse and this had been a much more severe pandemic, we may have needed to go that way anyway, because whatever risk around hesitancy might have been overcome by fear of the virus itself. But I don't think that's where we are. I do believe that we need to move expeditiously in preparation for any future pandemic to be able to better address these questions about adjuvants and other technologies.

Mr. STUPAK. My time is up.

Mr. Walden, for questions please.

Mr. WALDEN. Thank you very much, Mr. Chairman.

For those of us who don't spend our lives in the world you're in, can somebody give me like a 20-second explanation of an adjuvant? Doctor.

Dr. NARASIMHAM. Sure. Adjuvants have actually been used in vaccines in the United States since the 1920s. There's one called alum that's been used extensively. Adjuvants are actually additives that we put in the vaccine that actually boost the immune response. So, in this case, what we would do is we would make the vaccine as we normally would make it, add in the adjuvant, and then see how the vaccine performs. And typically a lot less vaccine is needed and the immune response is higher.

Mr. WALDEN. And in your clinical trials overseas did I hear you say correctly that you haven't seen any adverse response—well, maybe not any adverse response. You always have some. But nothing out of the band you would look at.

Dr. NARASIMHAM. In our clinical trials—I also just wanted to correct, we have now 25,000 subjects that are nonelderly. So it's not that we don't have data on elderly. We have quite a robust data set in the nonelderly population. We only see—we see reactions comparable to seasonal vaccine for adverse events.

Mr. WALDEN. And when in 2008 did you apply to FDA for approval?

Dr. NARASIMHAM. We did not apply—just to clarify, we did not apply for approval.

The first step is to file an IND, which would then allow us to take the steps to file for the approval. Our intention has been to use our European data to try to move forward. The question always has been how much data needs to be repeated in the U.S. that was done in Europe.

Mr. WALDEN. And when in 2008 did you do the first application?

Dr. NARASIMHAM. I can get back to you on the exact date. I think it was mid-2008.

Mr. WALDEN. And what else do you hear from FDA that you need to supply that you haven't?

Dr. NARASIMHAM. I think they would like to see adequately controlled, randomized studies under FDA oversight that demonstrate the safety and benefit of the vaccine. We have a lot of data. A lot of it—most of it has been generated not under FDA oversight, with EMEA European oversight. And the question for us as a company is how much of this can we realistically be expected to repeat. And, of course, with flu vaccines being as profitable—or not as profitable as they are—or as profitable as they are, which is to say they're not.

Mr. WALDEN. OK. So going back then—well, let me run this—if this were the feared Avian flu that we had hearings on and the potential of four out of every ten dying because of it, I guess we would declare some sort of emergency and take whatever risk there is. But if you're using this MF59 in Europe and you're not seeing any real problems, I just wonder what it would take here to get going on that. What does FDA—we should ask FDA.

Dr. NARASIMHAM. I can't speak for the agency. My understanding is, if the severity was such or if the unadjuvanted vaccines had not worked, they would have looked at this much more seriously. With H1N1, it's very difficult to get the unadjuvanted vaccines to work. So, hence, the MF59 becomes—adjuvants in general become much more important.

In this case, because they had an unadjuvanted vaccine that worked, I think they were more reluctant to move with the adjuvant. I would say that HHS and BARDA has funded a lot of our work with adjuvants so that the U.S. Government has supported a lot of the work that we've done.

Mr. WALDEN. But looking at it from where you are today with the FDA, what kind of time line do you think you and the FDA are on? And I realize they are your regulator and approver and you have to be really nice here. I don't mean to put you on the spot. Just for my sake and the public's sake, what kind of time line?

Dr. NARASIMHAM. The way we look at this is we have an H1N1 adjuvant, we have a seasonable adjuvant, and we have an H5N1 adjuvant. Our goal is to get ideally all of these licensed as soon as possible. We would be willing, of course, to file as soon as we can find a pathway with FDA that makes sense. But I think we would be unwilling to repeat large clinical studies and incur all the costs again, if that's what's ultimately going to be required, unless the government helped us.

Mr. WALDEN. Are we the only country that doesn't allow the adjuvant in our vaccine?

Dr. NARASIMHAM. At least for Novartis the only country that we do not supply adjuvanted vaccines to is the United States.

Mr. PERREAULT. If I could just comment. CSL has a unique adjuvant as well that we developed in Australia, and we did put it into the H5N1 that we supplied to Australia during that time frame a few years ago.

Mr. WALDEN. And H5N1 is what?

Mr. PERREAULT. That's the bird flu, Avian flu.

We also have multiple research programs going on with partner companies who are developing vaccines utilizing our adjuvant, and this adjuvant is being manufactured in Kankakee, Illinois.

Mr. WALDEN. It's manufactured here. We just can't use it here.

Mr. PERREAULT. It's being used in clinical trials with new vaccines that are being developed by other companies that we partner with.

Mr. WALDEN. And as you've used it in other countries, if I understood you correctly.

Mr. PERREAULT. We've done the studies for H5N1 in Australia.

Mr. WALDEN. And did you find any outlier effect?

Mr. PERREAULT. It was safe and efficacious.

Dr. NARASIMHAM. And we're also able to produce MF59 in the Holly Springs facility; and we expect the MF59 suite in Holly Springs, North Carolina, to be operational in December.

Mr. WALDEN. All right. My time is expired. I know we have other members here who want to ask questions. Thank you, Mr. Chairman. Thank you of the panel.

The CHAIRMAN. Chairman Pallone.

Mr. PALLONE. Thank you.

I was going to use my time with Dr. Lakey here because you're the State guy. And I don't know if you were here when I asked the first panel, but all my questions were about distribution and also about funding, because Dr. Lurie brought it up.

Basically, you know that CDC has left it up to the States to decide how to distribute the vaccine. So I wanted to know how a State decides which entities will distribute vaccine, you know, how many doses they receive; and, essentially, do you agree with the CDC that these decisions should be left to the States or should they be dictated by the Federal Government maybe a little bit more strictly?

I know they have guidelines, but—I don't know if you were here before, but I've been getting all these criticisms in New Jersey about the Wall Street firms getting the vaccine because they can distribute it better than some other places. And we're hearing in my own State of New Jersey and in New York about major disparities, one school district versus another that gets it, one gets it, the other doesn't. I just want your response. I know you're a State official, so you probably think States are great, but I would just like your response.

Dr. LAKEY. Let me provide some background related to how we do this.

We have the ACIP guidelines, the high-risk groups. And then those were further prioritized into a group taking it from 159 million to about 49 million. And so the challenge for us has been the changing landscape of how much vaccine is going to be available. Because your strategy to deliver a vaccine changes depending on how much vaccine you have. You can't run a mass vaccination clinic if you only have 100 doses, and you can't provide a school-based clinic if you're not immunizing healthy young kids.

And so States looked at those priority groups; and I think most States looked at health care workers, pregnant women, and very young kids as those top individuals that we needed to start our immunization program with. The challenge was that the first vaccine that was available was the nasal spray, and so we couldn't immunize pregnant women with the nasal spray.

Mr. PALLONE. Just to interrupt you, I've had that phenomenon, too, where one of my school districts has the nasal spray but doesn't have the vaccine and they want the vaccine instead of the nasal spray.

Dr. LAKEY. And so it's a matching of the vaccine you have available with your priority groups and your distribution system, what systems do you have available. And so a lot of us State health officials tried to move from large vaccination clinics to using the private sector.

Mr. PALLONE. So you use employers as well the way New York does?

Dr. LAKEY. Well, we're providing it to the physicians, the health care systems——

Mr. PALLONE. So you don't actually—I know I'm interrupting, but I'm running out of time. You don't actually do like what New York has done or maybe New York City has done, where they would go to large employers like Citigroup or Goldman Sax that have health clinics and have them do the distribution.

Dr. LAKEY. I have 13,000 registered providers on our system, and it's a combination of many of those. There may be some occupational health, but they're the minority. Most of these are pediatricians, ObGyn, family practitioners in the State.

Mr. PALLONE. Do you think that—I mean, I'm asking you to criticize another State, but, I mean, would you—New York obviously uses some of these large employers. Do you think that makes sense?

Dr. LAKEY. Well, I don't know the details of New York. From what I have gathered is that they have been trying to meet the priority groups and trying to reach pregnant women in different ways that they can do it, but I cannot speak for the State health officers.

Mr. PALLONE. Let me ask you this. You did mention the challenges of intermittent public health funding. And Dr. Lurie brought up funding challenges. I was a little critical because I don't remember the Secretary mentioning that when she was here. And, of course, if you need money, this is the place to come, for the most part, these days. Talk to me a little bit about that. I mean, to what extent the lack of funding or intermittent nature of it has been a problem.

Dr. LAKEY. Sure. I think there is a couple of issues here.

One is, the Federal funds that have been made available, you know, after 9/11, a lot of funds were made available, it peaked, and then it gradually declined. And so we receive now about half of what we were receiving earlier on.

We also had in 2006 one-time funding related to pandemic flu. And so that money was utilized to put together plans. But you can't hire people for long term on one-time funding, and so that funding went away. Those plans were made. But you can't continue that process after those funds have went away.

Mr. PALLONE. But you obviously feel that it makes sense for the States to have a lot of discretion here. In other words, you wouldn't suggest that the Federal guidelines be strengthened or made more detailed at this point. You believe the States should have the leeway to pretty much do what they want pursuant to the existing guidelines.

Dr. LAKEY. I guess, for clarification, that's for the folks that are being vaccinated right now——

Mr. PALLONE. In terms of the distribution.

Dr. LAKEY. The distribution system?

I think where we are right now folks are titrating up those groups. I think they base that on their capacity as a State. What were the resources? What was their history with delivering vaccine? And then they use those systems.

And so you have—public health is structured many different ways across the United States. And they use that uniqueness of their system, who they could reach the quickest, in order to determine their priority groups, using the same basic philosophy trying to get pregnant women, young kids, health care workers from the beginning, but then how they message that and adjusted that was dependent on what that State system was.

Mr. PALLONE. All right. Thank you. Thank you, Mr. Chairman.

Mr. STUPAK. Mr. Shimkus for questions, please.

Mr. SHIMKUS. Thank you, Mr. Chairman; and thank you to the panelists for being here.

We have spent a lot of time on adjuvant and how it boosts this. But I want to focus a little bit on the nasal spray. And so, Dr. Machielse, I know in your written and opening statements you mentioned the—I guess it's intranasal technology and the ability to get 80 to 100 versus 1 through 7 doses. Can you explain that to us and why that's—I mean, if we're talking about needing a lot of doses, from the layman's point of view it sounds like a good thing to be focusing on.

Mr. MACHIELSE. I can explain it. I think there are two reasons for that.

One is, I think we at MedImmune, we develop our own seed strain; and using the reverse genetics we can quickly screen multiple variants of the vaccine and select for growth properties immunogenicity. So, for instance, for the H1N1 vaccine, we basically screened 23 variants and did not lose any time; and we were in commercial production at scale on July 3rd.

I think the other important factor is—so we were able to actually immediately create an H1N1 strain which produces as much as we have seen in the past.

And then the other advantage of the live attenuated technologies is it is actually sprayed in the nose. The virus replicates there and creates an immunoresponse. So if you compare it to the inactivated vaccine you need a very, very small dose. Maybe if you compare it from—let's call it quantitative burst—a factor of 50 or lower. So I think that is a very important attribute, to actually consider this technology as part of pandemic preparedness. And I could tell you we have manufactured over 100 million bulk doses, and we could easily have gone up to 200 million doses by—bulk doses by the end of this year.

Mr. SHIMKUS. And what piqued my interest was also some of the comments when Chairman Pallone got into the discussion a little bit in the nasal spray issue is not for pregnant women. But there's a lot of other—I mean, the other two groups, there would be no prohibition for them, is that true?

Mr. MACHIELSE. That's correct.

Mr. SHIMKUS. I think he mentioned a school that didn't want to do nasal spray.

Mr. MACHIELSE. I think that we are not—you know, we do not have pregnant women in our label and we cannot administer the intranasal spray to that population. But the majority of the risk population is covered by the intranasal vaccine. So I think what's also very important is that there is enough education to actually objectively make people aware of the choices available in the flu

vaccination technology. Because maybe people now react on the intranasal vaccine, but it may be the same fear factor for the adjuvanted vaccine. And I think those assumptions in the public could be avoided by a targeted education campaign where it is emphasized that the safety and efficacy of the general vaccines available in the U.S. is good.

Mr. SHIMKUS. Thank you.

Dr. Lakey, the title of the hearing is An Update on Vaccine Production and Distribution; and when I initially read that I always think distribution is can a drug get from point A to point B. I think what a better title for this would have been in the decision-making matrix of who gets it. Not—for me—there is no distribution problem as far as you see when this is produced to delivery to an end point user, is there?

Dr. LAKEY. For the most part, no. There is—so that is in the private sector. It is manufactured, we order it, and it is shipped. That system seems to work for the most part. There have been weather events, et cetera, that have slowed that down, but for the most part that distribution system has worked.

Mr. SHIMKUS. What else do you think we need to do? Because you probably listened to the opening statements. My concern is, if we can't get this right, how do we do something? What do we need to do to prepare ourselves better for H5 or something that could—may turn out to be a bigger problem?

Dr. LAKEY. Well, I guess I've learned through other events, such as hurricanes, et cetera, that you have to take time afterwards to critically look at what went well and what you could have done better and just learning from your experiences.

I think there's been good discussion today of what we can do to improve the availability of vaccine. I think making sure that we communicate effectively to individuals' real expectations and not set artificially high expectations. Because I think the general public will respond when we give them the right expectations.

Mr. SHIMKUS. And I agree.

My time is expired. Thank you, Mr. Chairman. Thank you, panel.

Mr. STUPAK. Thank you, Mr. Shimkus.

Mr. Green for questions, please.

Mr. GREEN. Thank you, Mr. Chairman.

And, Dr. Lakey, I appreciate you being here and glad we got to meet earlier and appreciate what you've done for 3 years as the Commissioner of Health in Texas.

And I guess one of my interests is on the delivery system. Although our big issue here is why we don't have enough vaccines, obviously. And I know you experience it every day in Texas like a lot of us hear from our offices. But one of the challenges you mentioned is associated with school-based clinics and vaccinations. And I notice in today's Houston Chronicle some of my school districts in the Houston area are actually doing it—Alief, Humble. And I was wondering are you having any resistance from schools, particularly schools that have school-based clinics, to providing the H1N1 for their students?

Dr. LAKEY. I think what you are seeing in Texas is a mosaic of different strategies working together to get individuals immunized. I think some schools—there are school systems that have a lot of

experience with school-based clinics, and those seem to work. There are other school systems that haven't done that well, haven't done it in the past.

There are some challenges, making sure that you get parental consent so you don't immunize a child that hasn't provided consent, the parents haven't provided consent, and other just logistical challenges.

There are folks that you have to have there to provide immunizations, et cetera. We are using some of the funds that were provided by Congress to be able to hire individuals to allocate that.

But all those things have to come together. So that's one part of our system. We're able to do that now in Texas because as we've titrated up the number of groups we've been reaching the high-risk individuals, you know, the children with asthma, et cetera. And so we're now able to expand out to some of the healthy kids in our State.

Mr. GREEN. Can you tell us how public health emergency funds help you and other State public health departments set up and operate the H1N1 program?

Dr. LAKEY. Excuse me again, sir?

Mr. GREEN. How the public health emergency funds that you receive help with that.

Dr. LAKEY. The public health emergency funds came in three components, and they've been critical to our ability to respond.

The first part had to do with getting surveillance systems. Again, public health has been cut and so having feet on the ground in order to investigate cases, figure out whether it is H1 or not, that's been critical to hire those individuals.

We've been able to improve our laboratory capacity. Having the individuals in the laboratory to process samples, that has been a critical component of our system. We've been able to develop the vaccine ordering system in order to make sure that we have that technology in order to accomplish this.

About 81 percent of the funds that came in public health emergency response three we sent out to the local health departments so that they could hire the individuals to be able to respond.

Again there's been significant cuts at the local level in public health. A lot of those public health departments are shrinking and can't provide that investigation, the delivery of vaccine, all those different manpower components without the funds that were allocated in order to hire those individuals.

Mr. GREEN. Dr. Levi, I know you released a report coauthored with the American Academy of Pediatrics that states that school age children are the population most responsible for transmission of influenza and has the highest rate of attack. That report also sites in 2005 a school-based pilot program in the State of Maryland where FluMist was administered to children in several Maryland secondary and elementary schools and the results were that the program showed significant reduction in respiratory illnesses within households of children who received these vaccines versus schools that do not participate.

It seems like that report, and I am sure there is other proof that shows school-based facilities, of course, with the parents' permis-

sion, but that making it available to parents is a successful way to deliver that.

Mr. LEVI. Absolutely. And certainly using school-based facilities for both immunizations and the other types of health care are critically important. That is why there is some major provisions in the health care legislation that would expand that capacity. This is a tremendous opportunity to reach kids.

A lot of our pandemic planning assumed that kids would not be—it would be more like seasonal flu and the elderly would be most vulnerable. As it turned out, young kids were the most vulnerable. So if we had a strengthened school-based clinic and immunization program, we would certainly be in better shape today.

Mr. GREEN. Mr. Chairman, my last question actually is for the reason we are here, and it is to ask our producers of the vaccination, I know there has been a lot of discussion regarding benefits of new technologies to produce flu vaccines and the cell culture is the newest one. But I understand there is no difference, we wouldn't be producing faster vaccines using cell as compared to the eggs. And if each of you, as brief as you could, could respond to that, is there something we could do to make it quicker, whether it is eggs or the cell?

Mr. HOSBACH. Cell culture is not a game changer, and I think I will steal that phrase from Tony Fauci. The game changer probably is something along the lines of a universal flu vaccine, which you could stockpile that covers all different variants of flu strains over the course of seasons. However, that is a long ways away.

In terms of saving time, whether it is cells or eggs, you are, again, dealing with Mother Nature. You have to adapt the virus to the system that you are utilizing. And perhaps with cells make you save 2 or 3 weeks. But in terms of capacity and overall production capacity, I don't think it is really a game changer. You get vaccine out there about the same time.

In fact, the two facilities we have based in the U.S., they have the potential to produce 150 million trivalent seasonal doses. If you convert that to a monovalent, that is 450 million doses of an H1N1 type vaccine. So there is plenty of capacity right here on U.S. soil with the one new facility and our existing facility.

What we really need to look at why aren't we immunizing as many people as we should be immunizing on a season basis, when 36,000 people die every year and 200,000 people are hospitalized. We have recommendations from the ACIP that 275 million people should be immunized on an annual basis. We are lucky to immunize 100 million people.

If you want to sustain influenza immunization, production, development of new technologies, we really need to make sure we get more people immunized for the benefit of public health and for sustaining our manufacturing capabilities.

Mr. GREEN. OK. So the capacity is here, whether it is production in the United States, and I know we have one production in Australia, which is fine. But we have the capacity to produce 400 million vaccines?

Dr. NARASIMHAM. I think there is an important dynamic here for this vaccine. What we saw with the avian influenza is that an unadjuvanted 15 microgram dose was not sufficient. In fact, many

manufacturers thought it took 90 micrograms, right, which is six times as much, which means that the supply collapses.

So as the only manufacturer here that actually produces cell-culture-based vaccines, we actually have two licensed cell culture vaccines now in Europe. We are producing it for Europe, unadjuvanted and adjuvanted, seasonal and pandemic. And what our belief is with cell culture, you get some speed gain. Our expectation is a little different view is that it is on the order of 6 to 8 weeks, but it is not massive. I mean, it is going to be on that range as to the gain you get with cell culture.

But as Dr. Machielse also mentioned, with reverse genetics and using some new technologies, cell culture allows you to actually meet the need of many of the changing viruses that are out there. The worst case scenario for the American public is you rely on a single technology, that technology doesn't work when it is a different influence a strain, and then suddenly you have a real crisis on your hand.

So I think it is a wise strategy to invest in multiple different technologies, simply because we don't know how any one virus will behave.

Mr. STUPAK. Quickly, because we have to get to Mr. Burgess. We have votes here soon.

Dr. MACHIELSE. For us, you know, the eggs are working well. But I think if you can have the cell culture technology also available, it derisks the supply. In effect, if you have a really bad avian flu going around, it may affect the supply of eggs and those kind of things.

I think the scalability of cell technology is very critical, and I think especially if you think about the live attenuated flu technology. We have a facility in Frederick, Maryland, with two 2,500 liter bio-reactors. With the cell culture inter-nasal technology, we could manufacture half a billion doses in that facility. If you think about the cost efficiency you could generate, I think the cell culture at scale could be a very interesting asset and guarantee or further guarantee supply of flu vaccine.

Mr. STUPAK. Mr. Burgess, for questions.

Before you start, I should mention that you are one of the members that had written to myself and Chairman Pallone and asked for this hearing, along with other members. We appreciate it.

We will start with the questions.

Dr. BURGESS. You are kind to point out that I didn't whine.

You just finished up on an excellent point, Doctor. Mike Leavitt came and testified here in, I guess it was 2005, that it was going to be very, very difficult to develop the number of eggs that would be needed to produce the vaccines if we culled all our chickens the month before.

Let me just ask a couple of questions of all four of our manufacturers, and I would appreciate brief answers. But when in the sort of timeline that has been going on since last April, when did you find out about the delay? When did you really appreciate we were a month behind?

Mr. PERREAULT. I will respond first. I think that we did not, because we did not participate in the pandemic RFP that was put out by the U.S. Government a couple of years ago, our contract was a

bit different. So we started the negotiation in May and finished in May, which is the fastest I have ever done a government contract, by the way, which was quite nice to see. And we had to submit at that time our schedule that we assumed, based on average yields, when we signed the contract.

Within 3 weeks, we could see that the virus was not growing well. So we started at the beginning of June, and we could see the seed strains we had were not developing. In fact, they were a half to a third of what we expected. Again, our expectations were set on 10 years of seasonal assays. But as all of the manufacturers here will tell you, each new flu season is a new flu season. You just can't tell. And I think you have a medical background as well, or are a physician, so you understand that.

But I think we knew right away. We had weekly conference calls with HHS and BARDA, and we informed them and put a new delivery schedule in July.

Dr. BURGESS. So you did conference calls, and that would be in June?

Mr. PERREAULT. We communicated in June, and then put a new delivery schedule together in July based on our assumptions.

Dr. BURGESS. What was Novartis' experience?

Dr. NARASIMHAM. With Novartis, we saw the reduced yields in July. And I just would point out for clarity's sake, we actually can't confirm yields until we receive FDA reagents, and those reagents were really made available in August. But with initial testing, we saw the reduced yields in July. We communicated our situation weekly with HHS, as did all the manufacturers.

Dr. BURGESS. Well, MedImmune is different, but what about Sanofi Pasteur?

Mr. HOSBACH. Actually, it is the same for us in terms of realizing we first started out on a very conservative estimate in terms of yield of the virus, and it actually was about 60 percent of what we thought it was going to be, even on a conservative number. And we had weekly phone calls with BARTA–HHS and schedules were revised all throughout the way periodically as we gained new information.

Dr. BURGESS. Well, I am a little concerned, because I had some conversations in August with CDC and NIH and was given assurances that when school started, we would be well on our way to having, depending upon the approval process, well on our way to having satisfactory doses by mid-October. And that was kind of the timeline that I was laboring under.

Let me ask you a question. In the end of October, Secretary Sebelius at a Senate hearing said she was going to put out a call to the manufacturers to accelerate production, but I am going to assume you had already done so at that point, is that correct? Is there anything you did differently as a result of that call?

Mr. PERREAULT. At CSL, what we did is when we did receive the call, we took another look at our ability to fill and finish vaccine. Producing the antigen is one piece of it. Then you have to actually get it into a formulation and put it either into vials or syringes.

Our manufacturing plants for fill-and-finish of flu vaccine are inside plants that produce other therapies. So our CSL business includes protein plasma therapies for rare diseases. So we had to ad-

just our lines and our manpower in order to see if we could free up some manufacturing slots, and we did that.

Dr. BURGESS. You did that as a result of the call on October 29th?

Mr. PERREAULT. We were evaluating all along the way, but that was also a call to reinforce what we had been discussing with BARTA.

Dr. BURGESS. Let me just ask any of the manufacturers, was it problematic for you that you were at the point where you were gearing up for the seasonal flu and suddenly had this H1N1 task added to the equation?

Dr. NARASIMHAM. I think it was just a compression of the timelines. We had to complete our seasonal flu, at least for the case of Novartis, complete our planned season flu doses, which was what we were requested to do, and then we started in our case H1N1 in July, which obviously brings us to have a very short timeframe, a short runway to sort of get the plane off the ground.

Dr. BURGESS. But still there has been difficulty getting seasonal flu vaccine out. I know our community has been lacking for several weeks. Are we back on schedule with the seasonal flu?

Dr. NARASIMHAM. In our case, we completed our seasonal deliveries in early October.

Dr. BURGESS. Completed them. But the House physician here is out, for example. My Wal-Mart back home is out. I know I could get the MedImmune, and I should do that. But for the other vaccine, in our area it has been harder to come out. I know Dr. Lakey may know more about what difficulty we are encountering there.

Let me just ask MedImmune, on the issue of adjuvants, are there adjuvants that you use with your attenuated live virus?

Dr. MACHIELSE. We don't use any adjuvants.

Dr. BURGESS. Because your yield and the method of immunogenicity is such that the yield is so high?

Dr. MACHIELSE. It is live virus, and basically it replicates in the nasal cavity. You don't need an adjuvant.

I just want to highlight that we completed our seasonal manufacturing also in time and were even able to accelerate it to free up more manufacturing capacity for H1N1.

Dr. BURGESS. Thank you.

Dr. Lakey, let me just ask you, because Texas has had some problems, and some of them made their way into the front page of the newspapers. But when did you learn that Texas was going to be having some difficulty delivering on the vaccine shipments?

Dr. LAKEY. I think we learned as vaccine was coming out that it wasn't what we had anticipated. So in early October, as I recollect, was when we figured out that what we were being told we were going to get was not what we had been told in the past.

Dr. BURGESS. Do you feel that CDC and HHS shared information with you in a timely fashion?

Dr. LAKEY. We have had multiple calls with the CDC and the Office of the Secretary of Preparedness and Response, and they showed predictions, but a lot of them changed pretty quickly.

Dr. BURGESS. Now, have they been helpful in helping you adapt to the change in the vaccine availability?

Dr. LAKEY. The CDC has been very helpful to us in the State of Texas when there have been issues that have arisen. We have called them individually. We have conference calls two times a week with their leadership, with all the State health officers, to discuss issues and to have a question and answer time period. So they have been available and have answered questions.

Dr. BURGESS. And how about the manufacturers themselves? Have they similarly responded with information when you needed it, or do your communications go directly through CDC?

Dr. LAKEY. My communication would go through the CDC. The manufacturers would discuss that information with the CDC. So there hasn't been a direct conversation between State health departments and the manufacturers.

Dr. BURGESS. And you and Mr. Pallone talked a little bit about funding. Do you get the feeling that the level of funding, the $1.5 billion, was not satisfactory? Do you have an idea in mind of what would bring us to a level of funding that would be satisfactory?

Dr. LAKEY. So this is for the funding right now? The Association of State and Territorial Health Officials talked to State health officers to figure out what they think they would need. That survey thought that about $800 million would need to be available in order to continue this response through March.

Some State health departments are in better shape than others. Some, I believe about half of them, are predicted to run out of their FIR funding by the end of this year. So, again, State health departments are in different situations, but when we have tried to look at this systematically throughout the United States, the number was about $800 million to get all State health departments through the end of this pandemic.

Dr. BURGESS. Now, you have indicated to me that you see the number of cases has actually diminished over what it was even just a few weeks ago, and yet we are coming up to the holiday season between Thanksgiving and Christmas. People will be traveling a great deal in this country. I just remember my days in the clinics, you would typically see a great increase in viral syndrome around Christmastime and the weeks shortly after.

Now, could we anticipate a resurgence of the number of cases toward the end of the year because of the amount of travel people are going to be doing?

Dr. LAKEY. That is correct. So, as a State, we monitor the percentage of visits to physicians that are for influenza-like illness. We peaked in Texas around 13 percent. We have gone down to about 7 percent. But the nature of pandemics is they occur in waves and we predicts there will be a third wave. The challenge will be how that third wave corresponds to the seasonal flu. Do we hit one and then the other, or do we have seasonal flu on top of H1N1, which would be a challenge for State health departments.

Mr. STUPAK. Mike, I have to wrap it up.

Dr. BURGESS. Just as a final thought. We are right next door to Mexico, which is where this began a year ago. Is there any thought what might be happening to the evolution of the pandemic in Mexico? Will they be on their second, third or fourth wave around February or March, around the same timeframe this was introduced last year?

Dr. Lakey. I don't know if I can intelligently answer that. I think we predict they are going to have an additional wave. I think what we have—one of the challenges for us is there correspondence between the severity and socioeconomic factors? So in poorer areas of our State or in poorer countries, do we have more significant disease. So we are wrestling with that currently.

Dr. BURGESS. It definitely impacted us last year. When they became ill, we developed symptoms very quickly in our State.

Dr. LAKEY. Infectious diseases do not respect borders. It came across our border very rapidly, and throughout the southern part—the hardest part of Texas, the part of Texas that was hit the hardest, was our southern border. If you look at our fatality rates, et cetera, there is a significance difference of our border versus the rest of our State.

Dr. BURGESS. Thank you, doctor.

I yield back, Mr. Chairman.

Mr. STUPAK. Just to summarize, we are going to have votes in a few minutes, and we will finish up with the panel and finish up this hearing.

Dr. Lakey, it is fair to say we are going to get another wave of this H1N1? Right now, it seems like we are at a calm before the storm. Is that because there is more vaccines out there, or what is it? We are going to get hit again, are we not?

Dr. LAKEY. I am not sure if it is—there is probably several factors interacting. One, the natural history of pandemics coming in waves, and I think that is what we are seeing. And you will see differences across the United States. Activity is decreasing in Texas, it is rapidly increasing in other parts of the State, in the New England part of the Nation.

But the natural history of pandemics is they occur in waves. So our goal as we vaccine individuals is that we can blunt that third wave, and that is why it is not too late to immunize individuals. Even though this wave is decreasing, we need to block the third wave.

Mr. STUPAK. So as Mr. Burgess said, as we move about during this holiday season of Thanksgiving and Christmas, that could spread it in areas that have not seen the intensity we have seen in other parts of the country.

Dr. LAKEY. As we get into the colder season, as people are more inside, as the humidity changes, as the environment is more conducive to the spread of infectious diseases, it is likely there will be additional spread.

Mr. STUPAK. And then we could very well have the seasonal flu on top of it?

Dr. LAKEY. Exactly, sir.

Mr. STUPAK. OK. Let me ask you this question, just to summarize. It is my understanding from listening throughout this hearing there really was a pretty good cooperation with the government in working this one out between communications, coordinations, and even moving some contracts fairly quickly. Is that fair to say?

I mean, usually we are on the government, but it sounds like this time actually all the preparedness they have done for a pandemic has actually worked out fairly well. Is that fair to say?

You are all nodding your head "yes."

Mike, any other questions before we close it down? Wrong question to ask.

Dr. BURGESS. I am disturbed because Secretary Sebelius did indicate to us we would have the doses that we needed. And, again, my calls to the CDC and HHS, although they were off the record in August, yes, I got the information that they had studied what was happening in the southern hemisphere, it wasn't as bad as what they thought, but there were certain populations that would definitely be at risk, but not to worry, we would have the vaccine done and approved and in the hands of providers certainly by mid-October.

At that point, the fear was what if it is worse when the school year initiates on the first of September and we have to push this stuff out the door before the clinical trials are finished at the end of September. So I am still uneasy about all of that timeline.

My very first statement on this was when I had that very first conference call, I was worried that we were going to underestimate the severity of this virus, and, I mean, it is just incumbent upon us to constantly stay vigilant and not get complacent about our ability to fight it off.

Mr. STUPAK. There is no doubt we had rosy forecasts from the Secretary that has not held true. But I think between the low egg production of the virus and the condensed timeline and the great demand, it probably has led to the frustrations that we all feel, and that is the purpose of this hearing, to get to it. And I think we learned from this panel and the previous panel.

But overall, I think the government cooperation in working together and trying to resolve this has been pretty good, probably above par.

So with that, let me conclude this hearing.

That concludes all questioning. I want to thank all of our witnesses for coming today and for your testimony. The committee rules provide that the members have 10 days to submit additional questions for the record.

That concludes our hearing. This joint hearing of the Health and Oversight and Investigations Subcommittee is adjourned.

[Whereupon, at 3:06 p.m., the subcommittees were adjourned.]

[Material submitted for inclusion in the record follows:]

Congress of the United States

House of Representatives

December 15, 2009

Dr. Anne Schuchat
Director
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30333

Dear Dr. Schuchat:

Thank you for appearing before the Subcommittee on Health and the Subcommittee on Oversight and Investigations on November 18, 2009, at the joint hearing entitled "H1N1 Preparedness: An Update of Vaccine Production and Distribution".

Pursuant to the Committee's Rules, attached are written questions for the record directed to you from certain Members of the Committee. In preparing your answers, please address your response to the Member who submitted the questions and include the text of the question with your response, using separate pages for responses to each Member.

Please provide your responses by January 8, 2009, to Earley Green, Chief Clerk, in Room 2125 of the Rayburn House Office Building and via e-mail to Earley.Green@mail.house.gov. Please contact Earley Green or Jennifer Berenholz at (202) 225-2927 if you have any questions.

Sincerely,

Henry A. Waxman
Chairman

Attachment

The Honorable Marsha Blackburn

From the Reuters article: Dr. Anne Schuchat of the U.S. Centers for Disease Control and Prevention said 41.1 million doses of H1N1 vaccines are either available or have been delivered but that state and local health officials still face logistical problems. According to Dr. Schuchat, "We tried to let people know that bumps could happen, that managing influenza vaccine is always unpredictable." But the message "wasn't as well absorbed as we would have liked."

1. What do you think was the federal government's biggest misstep in the H1N1 vaccine process?

2. What were the lessons learned from the H1N1 vaccine distribution process?

3. What could your agency have done better to avoid the delivery and access delays to the H1N1 vaccine?

4. How have your best practices changed going forward to better prepare for an uninterrupted and consistent flu vaccine distribution?

1. What do you think was the federal government's biggest misstep in the H1N1 vaccine process?

Original projections of vaccine availability were based on the best information available from the manufacturers at the time and were revised as additional information become available. However, the realities of production posed unanticipated and unforeseeable delays. Potential production delays such as manufacturers changing delivery schedules due to country prioritization, extremely low production yields, prolonged seasonal influenza vaccine manufacturing campaigns, and day-to-day logistical and production line problems were not incorporated into our projections.

HHS has made every effort to be transparent throughout the process, providing estimates and projections of vaccine manufacturing capacity availability based on our most current knowledge of vaccine delivery logistics and information from vaccine manufacturers, with the necessary caveats that vaccine manufacturing has numerous variables, many of which are inherent in the science of the virus and beyond our control. Changes in projections reflected delays in vaccine availability and not reductions in the total amount that will be available.

2. What were the lessons learned from the vaccine distribution process?

CDC is in the process of developing an evaluation plan to enable us to identify as many lessons learned from the distribution process as possible. One specific area of note is the area of school-located vaccination. The number of school-located influenza vaccination clinics held for H1N1 vaccination is unprecedented and this approach holds much promise for efficient administration of seasonal influenza vaccine going forward. The majority of states conducted school clinics to varying degrees, and using a variety of approaches. We plan to identify factors that lead to high response rates, to describe different models for school-based vaccination and criteria for selecting a model given variation in local resources, and to understand challenges and successes associated with billing third party payers for vaccine administration. Other areas that we will examine include, determining the best ways of enrolling providers to participate in large scale vaccination efforts, factors that contribute to their satisfaction in the process to ensure continued participation for future emergencies, communications between public health departments and providers for coordination of response; whether choices related to types of settings towards which vaccine was directed (e.g. schools, public health clinics, provider offices) made a difference in terms of vaccination coverage ultimately attained. As vaccine distribution efforts continue, CDC will continue to identify promising practices and opportunities for improvement.

3. What could your agency have done better to avoid the delivery and access delays to the H1N1 vaccine?

The success of our response to a Public Health Emergency depends most of all on medical countermeasures for treatment and prevention of disease to help reduce the spread of infections, reduce health consequences, and ultimately save lives.

Secretary Sebelius has asked the ASPR to lead a review of its entire public health and emergency medical countermeasures enterprise, to be completed in the first quarter of this year. This review

will help us determine what could have been done better in our H1N1 vaccine response efforts. But another goal is a modernized countermeasure production process that promotes promising discoveries, more advanced development, more robust manufacturing, better stockpiling, and more advanced distribution practices.

The U.S. pandemic preparedness strategy for establishing a domestic manufacturing surge capacity to produce sufficient pandemic vaccine for the entire U.S. within 6 months of pandemic onset involves an integrated approach utilizing vaccine development and U.S.-based manufacturing facility building. Advanced development of new influenza vaccines using tissue culture, recombinant DNA, and molecular technologies is the foundation for providing more flexible, robust, and less-vulnerable ways to manufacture influenza vaccines. Further advanced development of antigen-sparing technologies for existing and new influenza vaccines using adjuvants provides opportunities to expand the vaccine manufacturing base multifold at different points towards the final surge capacity goal. Coupling the enhancement of existing U.S.-based manufacturing facilities that produce egg-based influenza vaccines with the building of new domestic facilities that will manufacture cell-, recombinant-, or molecular-based influenza vaccines is the natural extension to vaccine advanced development that will achieve the U.S. pandemic vaccine surge capacity goal.

The seeds planted thus far have borne the trees that will bear fruit in the next several years. Specifically, the HHS cell-based influenza vaccine program supports advanced development of six cell-based programs in 2005-06. Two of these vaccines are nearing completion of final clinical testing and are expected to seek U.S.-licensure in 2010-11. One of these two companies has started to build a plant for the production of cell-based vaccines here in the US with assistance from HHS. This facility may be available for vaccine production in less than two years in a pandemic emergency. Other cell-based vaccine candidates are earlier in the development pipeline.

In June 2009, HHS made its first award for advanced development of a recombinant vaccine. Recombinant and molecular technologies do not require growth of vaccine seed strains in an egg or a cell to manufacture vaccine and thus vaccine may be available much sooner after pandemic onset. It is projected that this first program will be licensed for use in the US in three years. A second request for proposals (RFP) was released in September 2009 to support additional recombinant and molecular influenza vaccine candidates; multiple proposals were received for review with contract awards expected early in 2010,

In early 2007 HHS made awards for three antigen sparing technology programs. These technologies reduce the amount of vaccine needed to vaccinate a person and thus increase the total supply. These technologies are in late stage of development with H1N1 vaccines and are expected to seek U.S.-licensure in 2010. In addition, support for the development of new influenza vaccine technologies and early clinical trials is ongoing through the NIH.

Additional new influenza vaccine manufacturing facilities in the U.S. would augment existing and nearly completed influenza vaccine manufacturing facilities implementing new cell-, recombinant-, or molecular-based technologies. HHS plans to issue a RFP in early 2010 to support the construction of a new facility in the U.S.

Additionally, new vaccine production technologies and technologies that expedite the vaccine production and delivery process will be pursued, such as new and faster ways to measure vaccine potency, which will provide better estimates of vaccine production.

Together these programs of advanced development and building domestic manufacturing infrastructure will enable the U.S. to meet its pandemic preparedness vaccine goals in the next three years.

4. How have your best practices changed going forward to better prepare for an uninterrupted and consistent flu vaccine distribution.

There are some important differences between the distribution of seasonal vaccine and the distribution of H1N1 vaccine. Seasonal vaccine is largely distributed through the private sector, i.e. providers order vaccine directly from distributors or manufacturers. The role of public health is limited, an important exception being that the vaccine is federally purchased through the Vaccines for Children (VFC) Program. Participating providers order vaccine through their state's immunization program for their patients under VFC. The same providers order vaccine directly from manufacturers and distributors for their patients who are not in the VFC program.

In contrast, the H1N1 vaccine has been distributed to vaccine providers under the direction of state and local health departments utilizing a provider agreement that CDC required be executed between state health departments and vaccine providers. Public health departments have been responsible for enrolling providers and then determining where allocated vaccine will be distributed within their state/jurisdiction. Providers placed orders with the state, not with manufacturers or distributors, and received vaccine as it was directed to them. States have had different approaches in terms of directing initial vaccine for public health clinics, practices, and/or school-located clinics. Thus, the timing of receipt of vaccine by providers was a function of each state's overall strategy and varied between states.

One of the challenges associated with seasonal influenza vaccination in recent years has been frustration of providers with delays in receiving vaccine, and year to year inconsistency in timing of vaccine shipments. Consistent and uninterrupted distribution of vaccine requires a consistent and uninterrupted supply of vaccine from manufacturers. HHS is working with industry to develop new technologies for vaccine development and production that will contribute to a more consistent supply.

Part of the evaluation described in Question 2 will include engaging providers and public health partners to identify the strengths and weaknesses of each system and ways in which lessons learned during the H1N1 vaccination campaign can be utilized to improve seasonal influenza distribution.

Some specific activities have already been identified to improve the seasonal influenza vaccine distribution process, for example: CDC can work more closely with manufacturers and distributors to ensure that vaccine is initially targeted for high priority groups such as persons in long-term care facilities. CDC, working together with the National Influenza Vaccine Summit stakeholders, can facilitate development of partnerships between pharmacies/big box retailers,

state and local health departments and other providers to reallocate vaccine in the event of a shortage.

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
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December 15, 2009

Mr. Paul Perreault
President, CSL Biotherapies. Inc.
1020 First Avenue
P.O. Box 61501
King of Prussia, PA 19406-0901

Dear Mr. Perreault:

Thank you for appearing before the Subcommittee on Health and the Subcommittee on Oversight and Investigations on November 18, 2009, at the joint hearing entitled "H1N1 Preparedness: An Update of Vaccine Production and Distribution".

Pursuant to the Committee's Rules, attached are written questions for the record directed to you from certain Members of the Committee. In preparing your answers, please address your response to the Member who submitted the questions and include the text of the question with your response, using separate pages for responses to each Member.

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Sincerely,

Henry A. Waxman
Chairman

Attachment

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CSL Biotherapies

January 7, 2010

The Honorable John Dingell
Chairman Emeritus
Energy and Commerce Committee
United States House of Representatives
2328 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Dingell:

Thank you for your follow-up questions regarding my testimony at the November 18, 2009 joint hearing entitled "H1N1 Preparedness: An Update of Vaccine Production and Distribution." I appreciated the opportunity to discuss what CSL Biotherapies is doing to fulfill our commitment to the United States population during this flu season.

Specifically, you had six questions that are listed below in which we provide answers.

1. *What were the major factors that impacted your ability to produce the expected yields of the H1N1 vaccine? What if anything, did the federal government do to help you overcome this obstacle?*

   The initial 2009 H1N1 vaccine virus seed strain that was provided to vaccine manufacturers by the New York Medical College in June 2009 (NYMC X-179A) produced lower yields in the early lots than expected (approximately one third to one half of an average H1N1 seasonal influenza yield). It must be understood that the production of influenza vaccine is a biological system and the constraints on the speed of availability of vaccine doses is related to the ability of the virus to be grown in the chosen substrate (i.e. eggs or cells). Each new virus is unique and the growth of a given virus is unpredictable. We calculated our original production and delivery estimates on our average H1N1 yield over the previous 10 seasons and made the Department of Health and Human Services (HHS) aware that those estimates were based on historical H1N1 yields, subject to change based on the new, novel H1N1 strain. These lower than expected yields resulted in discussion with HHS and a revised schedule for production.

   To address the low 2009 H1N1 vaccine yields, CSL immediately initiated a program to investigate improvements to yields including egg incubation temperatures and inoculation concentrations. CSL made a number of incremental improvements to the manufacturing process, resulting in an approximately 10% increase in yield over that initially obtained. On August 18, 2009, CSL received a new vaccine virus seed (NYMC X-181) from the New York Medical College, which was introduced into the manufacturing process on September 4, 2009. Yield improvements in excess of 80% compared to the previous seed (NYMC X-179A) were observed in the initial lots.

   Everything possible was done to maximize the yields using the original seed lots including discussions and recommendations with government and industry experts. That said, I would recommend that the U.S. government focus on producing a greater variety of seed lots and

doing that earlier in the influenza cycle. As we have seen, the poor yields resulting from the first seed lot provided by the New York Medical College had a significant effect on delaying production of H1N1 vaccine.

2. *Have you had the resources necessary from the federal government to manufacture the H1N1 influenza vaccine quickly and safely?*

CSL has been in close and regular contact with HHS, BARDA and the FDA regarding the development and delivery of our 2009 H1N1 vaccine for the U.S. since May of 2009.

These discussions addressed contractual matters, critical steps and milestones in clinical trials, vaccine manufacture, seed strain selection and yields, production schedules and delays, delivery schedules and regulatory requirements for the approval of our sBLA for the vaccine in the U.S. We are working with FDA (CBER) on vaccine lot releases and we are working with the HHS on distribution. We have also worked with the NIH on clinical trials. The development and licensing of the H1N1 vaccine required close communication with FDA.

I would characterize our relationship with the federal government as a close partnership in seeking to deliver H1N1 vaccine to the United States.

3. *Do you believe the federal government has been effective in communicating to the public the need and other critical information about the H1N1 vaccine?*

The 2009 H1N1 virus global pandemic developed rapidly and all governments responded quickly to this threat. Specifically, BARDA has been very good to work with in terms of quickly revising schedules. We have also worked with the federal government to quickly commence clinical trials to ensure vaccine efficacy – so yes, I would say the government has responded quickly to this pandemic in our work with them.

I am not in a position to judge the overall communications efforts to the public, but am aware that the government expended considerable effort on such communication.

4. *Do you believe the preparations taken for increasing your manufacturing capacity has adequately prepared your company for future and additional outbreaks?*

Currently, CSL Biotherapies is operating under a one-year special contract with the U.S. government providing pandemic vaccine for the 2009-2010 flu season. CSL Biotherapies does not have a long-term contract with the federal government to supply influenza vaccine for a pandemic. However, as a worldwide manufacturer of vaccines, CSL Biotherapies is certainly capable of rapidly preparing for any such need. Therefore, CSL Biotherapies is happy to enter into discussions regarding such a contract that would help us be able to supply for potential or future outbreaks beyond the 2009-2010 flu season.

As a year-round manufacturer of influenza vaccine, I believe CSL Biotherapies is well prepared for any future or additional outbreaks of H1N1 influenza virus.

In preparation for other potential pandemics, the use of a novel adjuvant such as our Iscomatrix adjuvant would have the potential to make more doses available. Our Iscomatrix adjuvant would need to be developed further and licensed for the United States in conjunction with influenza vaccine.

CSL Biotherapies has completed a ramping up of a new state-of-the-art syringe filling line at our Kankakee, Illinois facility. If the government were willing to provide financial assistance, we would consider building a vaccine formulation facility at the Kankakee site.

5. *If the 2009 H1N1 influenza mutates, do you believe your facility will be able to produce the appropriate vaccine in a safe and timely manner?*

I have the utmost confidence that CSL Biotherapies will be able to produce H1N1 vaccine in a safe and timely manner and fulfill any future contracts that may be entered into with the United States government.

Regarding, any mutation of the 2009 H1N1 influenza virus, all manufacturers of H1N1 vaccine are reliant on the vaccine virus seed that is provided to us by the contracted entity to the federal government (the New York Medical College this past year). However, as CSL Biotherapies manufacturers flu vaccine for the Southern Hemisphere as well, we might have some advanced notice as to potential changes or mutations of influenza strains. Of course, any such change or mutation that is identified will be immediately shared with the World Health Organization and other government bodies.

6. *What should the federal government be doing to support the development of cell-based manufacturing technologies?*

First and foremost, I would recommend that there be a focus on producing a greater variety of seed lots and doing that earlier in the influenza cycle. As we have seen, the poor yields resulting from the first seed lot provided by the New York Medical College had a significant effect on delaying production of H1N1 vaccine. In my view, this supersedes questions about cell-based versus egg-based technologies.

In addition, development and utilization of adjuvants could help to enhance the immune response and reduce required dosing, which would make more antigen available for additional vaccinations. A supportive environment for development of adjuvants with influenza vaccine could facilitate this advancement.

Egg-based technology is well-proven, and has an extensive safety and reliability record. Egg-based manufacturing continues to supply all of the world's seasonal influenza vaccine every year and continues to be far more reliable than cell-based technology. It is not at all certain that cell culture based manufacture will provide either faster timelines or greater yield.

The production of influenza vaccine, as opposed to many other drugs, is a biological system and as such the speed of availability of vaccine doses is related to the ability of the virus to be grown in the chosen substrate (i.e. eggs or cells) than any other constraint. It is not

always possible to ensure the virus will grow well. The same constraint applies in both egg and cell manufacturing systems. Indeed, there is little evidence that cell systems provide any greater benefit in terms of yield or timeliness of supply.

CSL Biotherapies has conducted research and has evaluated many cell lines which exhibited poor yield performance. More recently, CSL Biotherapies has commenced evaluation of a newer cell line that appears to show greater promise and options with this technology. If the U.S. government is interested in supporting the development of cell-based facilities, at a CSL site in the United States, we would be happy to discuss such an option.

Once again, thank you for the follow-up questions and please let me know if you would like to discuss further or address any other outstanding questions or concerns.

Sincerely,

Paul Perreault Sr.
President
CSL Biotherapies Inc.

ONE HUNDRED ELEVENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING

WASHINGTON, DC 20515-6115

December 15, 2009

Dr. Vas Narasimham
President, Novartis Vaccines USA
Novartis Vaccines and Diagnostics, Inc.
701 Pennsylvania Avenue, Suite 725
Washington, DC 20004

Dear Dr. Narasimham:

Thank you for appearing before the Subcommittee on Health and the Subcommittee on Oversight and Investigations on November 18, 2009, at the joint hearing entitled "H1N1 Preparedness: An Update of Vaccine Production and Distribution".

Pursuant to the Committee's Rules, attached are written questions for the record directed to you from certain Members of the Committee. In preparing your answers, please address your response to the Member who submitted the questions and include the text of the question with your response, using separate pages for responses to each Member.

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Sincerely,

Henry A. Waxman
Chairman

Attachment

The Honorable John Dingell

1. **What were the major factors that impacted your ability to produce the expected yields of the H1N1 vaccine? What, if anything, did the federal government do to help you overcome this obstacle?**

Yields in production of antigen from the virus seed strain were the largest factor that affected our production of vaccine supply, which had been estimated based on historical averages of seasonal influenza production. The initial virus seed strain supplied by government authorities produced extraordinarily low yields industry-wide in July when it was first used to manufacture H1N1 vaccine. Because of the uncertainty regarding yield at the time of contracting, the initial government order for the vaccine assumed the 5-year average seasonal average yield and provided flexibility in delivery dates to account for the significant uncertainty that existed at the time. Yields improved when a different virus seed strain was used, but final yields were not known until FDA reagents and calibration values were available in August and then re-calculated in September. As a result, final estimates for production volumes of vaccine to be manufactured were not known until late September. This led to changes in supply forecasts and stoppages in vaccine filling and ultimately affected the timetable for supply.

We collaborated weekly with four federal agencies through regular teleconferences on the status of our production and the impact that virus seed strain yield was having on production. Several federal agencies were working diligently with global public health authorities to identify and create new, and more effective, virus seed strains for vaccine production. When these efforts were completed, the U.S. Government expedited access to new virus seed strains to enhance our production capacity.

What we all learned during this process is important as we look to prepare for future pandemics. In particular:

- More manufacturers and research centers with expertise in influenza should be involved in the global effort to develop virus seed strains for production to leverage the best that science and innovation can bring to the pandemic situation.
- Collaboration between industry and government is critical in order to run initiatives in parallel to conserve time and make available to the public as many safe and effective vaccine doses as soon as possible.
- We have made a good start on expanding cell culture based production capacity and now the government/industry partnership must turn its attention to bringing other components of vaccine production, such as potency and sterility testing, into the 21st century era of biotechnology.

2. **Have you had the resources necessary from the federal government to manufacture the H1N1 influenza quickly and safely?**

Yes. The federal government has provided support in the following ways for the 2009 H1N1 pandemic vaccine production:

- Funding and supporting large scale clinical trials with unadjuvanted and adjuvanted vaccine through BARDA and NIH.
- Accelerating regulatory review and licensure for both vaccines and new production facilities.
- Providing early commitments for the purchase of bulk antigen and adjuvant.
- Providing commitments in the summer for fill finished vaccine.
- Supporting rapid product release testing by FDA.

Since 2005, Novartis Vaccines has established an extensive and highly productive collaboration with BARDA on pandemic preparedness, and we place the highest possible priority on working in partnership with the U.S. Government to address the United States' public health challenges. Through this partnership, Novartis Vaccines is collaborating with HHS-BARDA on four major efforts: clinical development of flu cell culture technology, clinical development of antigen sparing (adjuvant) technology, production for pre-pandemic stockpile supply, and design, construction and operation of a flu cell culture production facility in the United States. We are privileged to work in partnership with the U.S. Government on these preparedness initiatives, all of which served us well as we confronted the challenges associated with the H1N1 pandemic.

3. Do you believe the federal government has been effective in communicating to the public the need and other critical information about the H1N1 vaccine?

Yes. The U.S. Government managed an unprecedented effort undertaking to produce, test, and deliver a safe and effective H1N1 vaccine to U.S. citizens despite tremendous challenges and compressed timelines, all the while preserving the integrity of the seasonal influenza campaign. Decisions were made in real time when not all data was available and sound choices were made on the basis of the best scientific and public health expert opinion. Additionally, the U.S. Government had to balance these decisions with growing anxiety in the American public about vaccine safety and increasing criticisms from a vocal and growing segment of the American public which opposes vaccines and vaccination campaigns. It was a difficult process to manage, but in our view the U.S. Government made decisions in the open and communicated them consistently to the American public.

4. Do you believe the preparations taken for increasing your manufacturing capacity has adequately prepared your company for future or additional outbreaks?

Yes, once we complete construction of our new Holly Springs, North Carolina facility. Since 2007, Novartis Vaccines has invested almost $1 billion in pandemic preparedness. There are two investments that address U.S. influenza vaccines: our $200 million recently approved Site 4 bulk manufacturing facility in Liverpool, England (which is where influenza vaccines for the United States are currently produced by Novartis

Vaccines) and our investment in our flu cell culture ("FCC") facility being constructed in Holly Springs, North Carolina in partnership with HHS. From our experience manufacturing cell culture-based influenza vaccines for use in Europe, these vaccines provide three principle benefits: faster production, better matched vaccines, and no reliance on eggs. FCC manufacturing in the U.S. will position the our nation to enable a more rapid response for any future pandemic. With the 2009 H1N1 pandemic, we were able to expedite vaccine production by weeks; our clinical trials were initiated in early July and on September 4th we provided U.S. officials with the first clinical trials data on H1N1 from our FCC trials.

In addition, Novartis Vaccines' development of adjuvant technology and capacity have prepared it well for future or additional outbreaks. Outside of the U.S., Novartis Vaccines exclusively provided MF59 adjuvanted H1N1 vaccine to other governments that secured vaccine from us. Novartis Vaccines has pioneered the study and use of influenza adjuvants over the past decade. MF59 is Novartis Vaccines' proprietary and patented adjuvant that is added to influenza vaccines to help stimulate the human body's immune response. In over 10 years of licensed use in Europe and experience in over 200,000 clinical trial subjects, Novartis Vaccines has demonstrated the following benefits of adjuvanted influenza vaccines: improved immunogenicity, antigen sparing maximizing the number of doses available through use of lower amounts of the antigen, cross protection against "drifted" strains, and cross priming to provide extended protection against newly circulating strains. The safety profile of adjuvanted influenza vaccines is comparable to unadjuvanted vaccines.

Novartis Vaccines has expanded manufacturing capacity for our proprietary adjuvant, MF59, to provide stockpiles as well as expanded production. Our newly established influenza vaccine manufacturing site in Holly Springs, North Carolina includes an adjuvant manufacturing suite, the first in the United States.

Finally, the 2009 H1N1 pandemic provided the opportunity to identify key challenges that need to be addressed in partnership with the U.S. Government to more fully prepare for future or additional outbreaks. These include:

- Continued investment in new technologies for production of vaccine and adjuvants.
- Regulatory pathways for novel technologies and creation of a mock up procedure, similar to Europe, to expedite the regulatory approval process.
- New processes for vaccine potency and sterility testing.
- Sustaining the stockpile production in the U.S. to assure adequate supply capacity.

5. If the 2009 H1N1 influenza mutates, do you believe your facility will be able to produce the appropriate vaccine in a safe and timely manner?

Novartis Vaccines is in a position to supply vaccine to the U.S. for any mutation that may occur as long as the virus seed strains are developed and are amenable to manufacturing

and we receive guidance from the U.S. Government about how to proceed in the context of seasonal vaccine production.

Based upon the advice of public health experts, for the 2009 H1N1 pandemic the U.S. Government weighed the risks and benefits of providing adjuvanted or unadjuvanted vaccine to the American public. We supported the government's decisions based upon the range of issues it considered in an effort to make the immunization campaign a success. However, as mentioned above, our research data on the use of adjuvanted vaccines, for both seasonal and pandemic production, demonstrates that our proprietary adjuvant provides cross protection when or if a virus mutates. Should the U.S. decide to proceed with an adjuvanted pandemic vaccine at some point in the future, we have the manufacturing capacity to supply such a product.

6. What should the federal government be doing to support the development of cell-based manufacturing technologies?

Novartis Vaccines has been a leader in developing and manufacturing influenza vaccine in cell cultures, and our flu cell culture product Optaflu was approved for use in Europe in 2007. Pioneered by Novartis Vaccines, flu cell culture manufacturing represents the first innovation in inactivated influenza vaccine production in over 50 years. It offers flexibility in the manufacturing process as the vaccine product is incubated using the tools of biotechnology rather than eggs. Cell culture-based vaccines provide three principle benefits: faster production, better matched vaccines, and no reliance on eggs. Our adjuvanted cell culture H1N1 vaccine was first produced in early June 2009, met all relevant regulatory criteria after extensive clinical testing, and has been approved for use in Switzerland and Germany with other country approvals expected shortly.

We are presently working in partnership with the U.S. Government as part of its pandemic preparedness effort to develop this technology for the United States, and have recently completed construction of our FCC manufacturing facility in Holly Springs, North Carolina, which we expect to be licensed to provide cell culture-based vaccine for the 2013-2014 influenza season. Support of FCC technology being fully optimized in the U.S. is dependent upon the following factors: a strong working relationship with the FDA to validate the newly constructed facility, expediting U.S. regulatory approvals using FCC clinical trial data that has been considered in the EU for approvals by the European Medicines Agency and continuing to support process improvements to keep FCC technology cutting edge.

MedImmune

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January 8, 2010

VIA HAND DELIVERY AND E-MAIL
The Honorable Henry A. Waxman, Chairman
House of Representatives Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515-6115

RE: Response to Committee Letter of December 15, 2009

Dear Chairman Waxman:

Thank you for the opportunity to appear before the Subcommittees on Health and Oversight and Investigations on November 18, 2009. I am in receipt of your letter dated December 15, 2009, requesting responses to certain questions asked by a Member of the Committee for the record. The responses to those questions are attached.

If the Members of the Committee have any further questions, please do not hesitate to contact me directly or through Vanessa Procter on our Federal Government Affairs team at (202) 349-9834 or procterv@medimmune.com.

Very truly yours,

Ben Machielse, Drs.
Executive Vice President, Operations and
Chair, MedImmune H1N1 Response Team

cc: The Honorable John Dingell

William C. Bertrand, Jr., Executive Vice President and General Counsel
Atul Saran, Vice President and Deputy General Counsel
Vanessa Procter, Associate Director, Federal Government Affairs

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January 8, 2010

VIA HAND DELIVERY AND E-MAIL
The Honorable John Dingell
House of Representatives Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515-6115

RE: Response to Questions Following Joint Hearing of Subcommittees on Health and Oversight and Investigations Entitled "H1N1 Preparedness: An Update of Vaccine Production and Distribution" on November 18, 2009

Dear Congressman Dingell:

The following are MedImmune's responses to the questions you raised following the above referenced hearing:

Q1: What were the major factors that impacted your ability to produce the expected yields of the H1N1 vaccine? What, if anything, did the federal government do to help you overcome this obstacle?

A1: MedImmune did not experience any negative impact with respect to expected yields of H1N1 vaccine; in actuality, the growth of our H1N1 vaccine outperformed our seasonal vaccine with regard to yields.

Within days of the initial outbreak of the H1N1 virus in late April, MedImmune began its development efforts to create a master virus vaccine seed that would grow well in eggs. Using the proprietary live, attenuated master donor strain that we use seasonally for FluMist® and our patented reverse genetics techniques, we were able to screen 23 different strains of potential vaccine candidates to isolate the one that had the best characteristics; the selected seed was sent to our large-scale bulk manufacturing facility on July 3, 2009. The manufacturing yields of this strain were comparable to or better than yields we normally obtain for our seasonal vaccine, averaging approximately 90 doses of vaccine per egg. Accordingly, we produced all 41.9 million bulk vaccine doses ordered by the government by September 10, 2009 and we produced over 100 million bulk vaccine doses by December 3, 2009, when we shutdown that facility to get ready for the 2010-2011 season.

Due to the emerging public health threat and need for expeditious vaccine development, MedImmune assumed the risk of producing H1N1 vaccine prior to the receipt of a contract from the U.S. Government. Contractual commitments were made at the end of May, in mid-July and in mid-September. We do not believe the federal government could have done anything more to accelerate our production of bulk vaccine.

The MedImmune influenza vaccine is administered as a nasal spray and so must be filled into specialized sprayers and its packaging and labeling must be approved by the FDA. We have been faced with three major challenges in this regard: (1) supply of sprayers; (2) the capacity of our filling and packaging lines; and (3) timely FDA clearance of our proposed packaging and labeling.

With respect to the supply of sprayers, MedImmune contacted the exclusive supplier of these sprayers early in the vaccine development process and was able to obtain commitments to provide up to 52 million sprayers in time for vaccine delivery between September 2009 and March 2010. The federal government ordered 41.9 million doses for delivery between September 2009 and February 2010. We delivered the first finished doses on September 22, 2009, and 29.5 million doses by December 31, 2009. We were still on track to provide all 41.9 million finished doses by February 26, 2010, but on January 1, 2010, HHS asked us to halt our finishing and packaging for two weeks while they assess the overall supply and demand of vaccine.

Regarding the capacity of our filling and packaging lines, MedImmune has been working for several years under contract with the U.S. Department of Health and Human Services (HHS) (Contract No. HHSO100200700036C) to retrofit our existing facilities to serve as a warm base of operations if needed in a pandemic to produce a surge of vaccine. As a part of those efforts, MedImmune had initiated work to add a second, high-speed filling line to its blend/fill/finish manufacturing facility. Although putting this new line into service was originally scheduled to occur in mid-2010, we were able to work with HHS and the FDA to accelerate licensure and initial release of doses from this new line to November 2009. These efforts, particularly the timely review and approval by the FDA, have been critical to staying on track with delivery of doses. We also temporarily shutdown our manufacturing facility in Frederick, Maryland, to reassign approximately 45 employees to assist with these efforts, and augmented our workforce by about 240 temporary personnel in order to allow for the 24/7 operation of the facility in three full shifts. Operating on a 24/7 basis has meant that minor mechanical failures (usually repaired within hours), difficulty accessing the facility due to the snowstorm on December 19-20, 2009, or other similar occurrences, have had some minor effects on the week-to-week schedule, but overall we have still been releasing several million doses per week as anticipated.

Finally, with respect to FDA clearance of our packaging and labeling, several policy discussions were underway among various government agencies regarding package insert requirements during the time in which we needed to begin packaging our product insert in order to meet the necessary timelines. When we did finally receive FDA clearance of the package insert we augmented our workforce by about 25 temporary personnel for six weeks who took shifts in subzero temperatures (required for product storage at that stage of the manufacturing process) to insert the approved labeling into the pre-packaged boxes. These additional efforts enabled us to continue to manufacture the product on the anticipated timeline.

Q2: Have you had the resources necessary from the federal government to manufacture the H1N1 influenza [vaccine] quickly and safely?

A2: Yes. The speed of production is discussed in the response to the previous question. With respect to safety, for our seasonal influenza vaccine, we generally conduct certain animal tests and one study in human adults. For our H1N1 vaccine, we conducted all the same studies in animals and adults and also, at the FDA's request, conducted one additional study in the human pediatric population.

Q3: Do you believe the federal government has been effective in communicating to the public the need and other critical information about the H1N1 vaccine?

A3: HHS and CDC provided good information to the American public about the precautions that should be taken to limit the spread of disease. HHS and CDC have also provided significant information about the availability of vaccine, although this transparency has meant that delivery schedule adjustments have required revising public expectations on a regular basis.

From a broader perspective, much of the lay public and health care providers misunderstand the relative risks associated with vaccination in relation to its benefits and do not understand the benefits of newer technologies, such as with MedImmune's live, attenuated nasal spray vaccine. We believe that correcting these misperceptions is a longer term effort that would benefit from additional education campaigns. Specifically, many high-cost, highly visible government communications have urged the public to get "flu shots" or "roll up their sleeves," which has the unintended consequence of dismissing the availability and significant role of the nasal vaccine in the current pandemic response and seasonal vaccination. Consistent education over many years would be beneficial to protect against the circulating virus each season, and importantly, would also be of significant benefit in terms of preparing the American public for the next pandemic.

We also note that if the federal government intends to control all vaccine distribution in future pandemics as it did this year, it needs to have a comprehensive plan for communicating the need for vaccination. In particular, the government would be well-served to spend time understanding the commercial marketplace for seasonal vaccine, both because it can elicit significant guidance as to market segments specifically needing education and because the commercial market for seasonal product can have an effect on the delivery and uptake of pandemic vaccine. For example, some health care payors provide lower rates of reimbursement to health care providers for services associated with the administration of our seasonal nasal spray vaccine than for the services associated with the administration of the injectable vaccine. Where that is the case, health care providers have a financial incentive to administer injectable vaccine rather than our nasal spray on a seasonal basis. This disparity also affects the uptake of pandemic vaccine because certain points of vaccine distribution, such as large chain retail pharmacies, may be reluctant to create public demand for a nasal spray if it might affect their earnings on that product. In addition, any pandemic vaccine distribution plan that includes state or private payor reimbursement of vaccine administration services to health care providers is likely to mimic seasonal vaccine distribution, and thus to provide a similar financial incentive towards usage of the injectable vaccine. Finding solutions to anomalies such as this in the seasonal market can therefore improve vaccination rates in the pandemic context.

Q4: Do you believe the preparations taken for increasing your manufacturing capacity has adequately prepared your company for future or additional outbreaks?

A4: As discussed above, we have the capability to rapidly develop a master virus vaccine seed using our proprietary technology and that this technology allows us to efficiently screen many potential vaccine candidate seeds. However, in future influenza pandemics, it will still be unknown whether the vaccine strain will grow in eggs well or at all. Accordingly, we believe it is still important from a public health standpoint that additional investments are made in cell-based and other novel technologies to allow for greater certainty in the manufacturing process. With respect to cell-based technologies in particular, please see our response to question number 6.

Since our vaccine is also limited by the number of sprayers available and the speed with which they can be filled and packaged, these are key considerations for future pandemics. To that end, as a pandemic preparedness measure, we would recommend a greater dialogue between HHS and vaccine manufacturers as to government's production expectations in the case of a pandemic. We would also welcome the opportunity to discuss preparedness planning more broadly and establish a shared blueprint with the government, both to make sure vaccine capacity is appropriately allocated as well as to provide any input or feedback based on our commercial experience. To the extent it is determined that public health efforts for pandemic planning require manufacturing capacity above and beyond normal commercial needs, we believe the federal government has a role to play in ensuring that additional production lines are available. We also believe that public health efforts could benefit from increased attention to the logistics of distributing vaccine once it is manufactured and that the government may be able to draw upon the experience of vaccine manufacturers in the commercial setting.

Specifically for our vaccine, in the next 1-3 years, we would also recommend creation of a government-supported stockpile of nasal sprayers for surge use in a pandemic. Longer-term, we believe it will be possible to develop alternative delivery devices that can reduce the time and cost of producing large quantities of vaccine quickly. For example, MedImmune is currently undertaking research and development of heat-sealed plastic bulbs (referred to as "blow-fill-seal" devices); although approval for such a device is likely several years away. MedImmune has also developed a concept-version ten-dose vial which would be packaged in a kit with ten disposable, single-use droppers. This approach could allow for the packaging and distribution of large quantities of vaccine quickly and efficiently. In evaluating the cost and potential viability of such a product on a seasonal basis, we do not believe this an approach that has a favorable commercial cost-benefit profile, but since it could be extremely useful in critical public health situations, such as for a pandemic, we have submitted a proposal to HHS and FDA to consider this approach.

Q5: If the 2009 H1N1 influenza mutates, do you believe your facility will be able to produce the appropriate vaccine in a safe and timely manner?

A5: If the 2009 H1N1 wild-type virus mutates in a similar manner as seasonal influenza strains, we believe that our live, attenuated vaccine potentially confers at least partial protection, as has now been shown for our seasonal vaccine through four published efficacy studies.

To the extent a new vaccine would be required, consistent with the response to the preceding question, we believe we would be able to develop a master virus vaccine seed reasonably quickly. However, if mass vaccination with a new strain is required in 2010

or 2011, we are not likely to have a significant inventory of sprayers available as we did this year. Accordingly, the number of doses we could provide would be significantly limited unless one of the alternative delivery devices described above could be approved rapidly or authorized for use on an emergency basis.

Q6: What should the federal government be doing to support the development of cell-based manufacturing technologies?

A6: The primary issue surrounding development of cell-based manufacturing technologies is the investment of time and cost required to refine the process. The time and cost are driven in large part by the human clinical studies the FDA has indicated would be required to show safety and efficacy. We are firmly of the opinion that appropriate safety studies need to be conducted, and believe that efficacy can be established by an approach that combines establishment of comparability of the cell-based and egg-based live attenuated vaccines with the many years of data that have been developed using egg-based vaccines, since the cell-culture and egg-based vaccine strains would be the same. However, we believe the extensive clinical data the FDA has required us to gather does not add meaningful information about the safety of the vaccine and does not enable a clear assessment of the risks and benefits associated with large-scale utilization.

From a broader perspective, the FDA's general approach to vaccine development mirrors its approach to drug or biologic development, namely that the onus is upon the manufacturer to establish a development plan and the FDA reviews the development plan at each phase of the program. Development of prophylactic vaccines that have a strong public health component, exemplified by influenza vaccines, and in which the federal government has identified a national risk, can and should be viewed independently. More specifically, public health would benefit from a more transparent dialogue among government public health advocacy groups, such as BARDA, the FDA, and industry in addition to key opinion leaders in the specific field. This transparent dialogue would allow for a more robust and conclusive discussion of the public health needs including any attendant risks and benefits. This, in turn, would allow manufacturers to establish a comprehensive, mutually agreeable licensure pathway that is based on thoughtful regulatory science, saving significant time and cost in the event of an emergency such as the 2009 H1N1 pandemic. The ability to develop this type of relationship will likely require additional resources for the FDA and HHS.

We hope that these responses have addressed the questions you raised. If we can provide any additional clarification to any of the responses above or to any addition questions, please do not hesitate to contact me directly or through Vanessa Procter on our Federal Government Affairs team at (202) 349-9834 or procterv@medimmune.com.

Very truly yours,

Ben Machielse, Drs.
Executive Vice President, Operations and
Chair, MedImmune H1N1 Response Team

cc: William C. Bertrand, Jr., Executive Vice President and General Counsel
Atul Saran, Vice President and Deputy General Counsel
Vanessa Procter, Associate Director, Federal Government Affairs

sanofi pasteur
The vaccines division of sanofi-aventis Group

Written Responses to Follow-up Questions

From the Honorable John Dingell

To

Phil Hosbach, Sanofi Pasteur

Regarding November 18, 2009 Hearing

Before

The House Energy and Commerce Committee

Subcommittees on Health and Oversight and Investigations

sanofi pasteur . Discovery Drive . Swiftwater, Pennsylvania 18370 . Tel.: 570-957-7187 . www.sanofipasteur.us

1. ***What were the major factors that impacted your ability to produce the expected yields of the H1N1 vaccine? What, if anything, did the federal government do to help you overcome this obstacle?***

The initial low productivity of the H1N1 seed virus was the principal constraint on production at the beginning of our manufacturing campaign. With each new influenza virus, it is necessary for the government to prepare seed strains, with the appropriate H1 and N1 proteins, that would be suitable for vaccine production. As often happens with seasonal influenza, the initial yields from the seed strains can vary significantly and are not fully known until manufacturers are able to utilize them in their laboratories. H1N1 yields were exceptionally low. Productivity of the H1N1 seed virus that was provided by the government was improved over time through application of Sanofi Pasteur's expertise in adapting seed viruses to our manufacturing process. Thus, yields are now similar to those traditionally seen for the annual seasonal influenza vaccine and H1N1 yields are no longer a significant factor impacting production schedules.

There were other, more minor, factors that affected the early delivery schedules for H1N1 vaccine. They are outlined in the testimony submitted at the hearing and in the Company's written response to questions provided in advance of the hearing.

The production of any influenza vaccine is a complicated biological process, involving many steps. In this case, the major obstacle was the nature of the virus itself. As was stated at the hearing, Sanofi Pasteur continues to believe that the US response to this pandemic has been a remarkable achievement. Thanks to the close collaboration of industry with HHS and CDC, we were better prepared for this pandemic than we would have been at any other time in history.

2. ***Have you had the resources necessary from the federal government to manufacture the H1N1 influenza quickly and safely?***

There has been, and continues to be, an extraordinary level of interaction between Sanofi Pasteur and the US government during the H1N1 influenza outbreak. Since April, when the H1N1 virus was first recognized, we have had weekly teleconferences with HHS/BARDA, the CDC, FDA/CBER and NIAID to discuss the issues and to coordinate and maximize the available resources. In particular, CBER has been very attentive to the review of our regulatory submissions relating to required filling lines and other facility issues. They have been very responsive in acting on these documents.

This collaborative approach can be credited with some early successes. For example, through close coordination with FDA and HHS, we were able to accelerate the licensure of two new filling lines in our new Formulation and Filling Facility at our Swiftwater, PA location – one of which was not scheduled to be licensed until 2010.

This level of collaboration with the federal government is not new for Sanofi Pasteur. In 2004, we began working with HHS on early pandemic planning. This groundwork has proven critical to our response to the H1N1 virus. For example, one of the most important steps toward preparing for an influenza pandemic was to put continuous egg supply contracts in place for vaccine producers. This critical forethought by the US government has allowed our company to manufacture influenza vaccine on a year-round basis.

Finally, we believe that Congress should be commended for having the foresight to provide the funding necessary to make the response to the pandemic as effective as it has been. It is important that we continue to

be vigilant in ensuring that our pandemic preparedness efforts are funded at levels at which they can be most effective.

3. Do you believe the federal government has been effective in communicating to the public the need and other critical information about the H1N1 vaccine?

From the outset of the H1N1 influenza epidemic in April, we were very encouraged by the extensive efforts of all levels of government, to communicate the complex issues relating to the H1N1 outbreak to the general public. These issues ranged from the epidemiology, the severity of the disease in particular populations and, eventually, to messages about the availability of a safe and effective vaccine produced in the same way that seasonal vaccines are made. In particular, the efforts of the CDC in providing daily updates across the spectrum of issues on both the internet and through webcasts has provided a substantial amount of information to the public, healthcare providers and industry.

4. Do you believe the preparations taken for increasing your manufacturing capacity has adequately prepared your company for future or additional outbreaks?

As mentioned in Question 2, Sanofi Pasteur, together with US and world health authorities, has been preparing for an influenza pandemic for many years. As the recent H1N1 pandemic has taught us, "capacity" is actually a composite of both physical (manufacturing) and human resources. Many of the plans relating to the management of our site and our human resources have now been tested and some important lessons will be used to further improve our crisis implementation process.

With respect to our facilities, we have two licensed influenza vaccine manufacturing facilities operating in Swiftwater, PA, the second of which was licensed by the FDA on May 6, 2009. It represents a 140,000-square-foot, $200 million corporate investment in domestic influenza vaccine manufacturing capacity. When running at full capacity, this facility should produce approximately 100 million doses of the three-strain seasonal influenza vaccine per year. In addition, our existing influenza vaccine manufacturing facility is capable of producing 50 million doses of the three-strain seasonal influenza vaccine per year, and through an existing contract with HHS, we intend to retrofit and extend the life of our older bulk production facility.

As mentioned in Question 2, the FDA has licensed several additional filling lines at our facility, which has expanded our ability to finish and fill product. This could not have been accomplished without the collaboration, diligence and focused efforts of Sanofi Pasteur and the FDA.

With respect to our human resources, it should be noted that more than 2,000 people at our Swiftwater facilities are in some manner involved in responding to the pandemic through development, production, testing and distribution of H1N1 vaccine. Our production facilities are running at their full licensed capacity, 24 hours a day, 7 days a week, with many of our employees making exceptional personal sacrifices to develop, produce and deliver vaccine as quickly and carefully as possible.

Again, as mentioned in Question 2, a critical factor in our ability to produce pandemic vaccines for future outbreaks is the year-round availability of eggs. The existing egg supply contract expires in April 2010 and we would urge the Committee to support HHS/BARDA's intentions to competitively renew this contract, so that premium-quality eggs are available 365 days a year. This egg supply will provide the necessary flexibility to respond to pandemic vaccine production at any time of the year.

It should be noted, however, that our experience with H1N1 is not necessarily indicative of our ability to respond to other viruses with pandemic potential. Unlike avian H5N1, for example, H1N1 2009 is highly immunogenic without the requirement for an adjuvant and only a single standard dose (15 mcg) is required in individuals older than 9 years of age.

It is important to understand that if the next pandemic virus is poorly productive, unstable upon formulation, less immunogenic or of widely differing antigenic types, the "capacity" that has been applied to the current H1N1 pandemic may be insufficient in terms of the timely delivery of a vaccine.

5. If the 2009 H1N1 influenza mutates, do you believe your facility will be able to produce the appropriate vaccine in a safe and timely manner?

As the largest and most reliable manufacturer of influenza vaccine in the US and abroad, Sanofi Pasteur is committed to producing all vaccines in a safe and timely manner and in full compliance with the legal and regulatory requirements of public health authorities. If the H1N1 virus were to mutate and the government were to call upon us to produce a different H1N1 vaccine, we would approach this new task with the same diligence and transparency as we have approached the current effort.

From a technical and regulatory perspective, if the H1N1 virus were to mutate, we anticipate that we could produce a new H1N1 vaccine using our licensed process, just as was done for the current H1N1 strain. However, if the mutations were substantial, it may be necessary for the government to create a new seed virus and for the company to replicate all of our work to prepare a new egg-adapted working seed virus. All of these are time-consuming activities and the productivity (yield) of the new strain would be uncertain, so there could be a delay in the availability of the "new," better matched H1N1 vaccine. There should be no expectation that there will be immediate availability of a new vaccine.

6. What should the federal government be doing to support the development of cell-based manufacturing technologies?

As stated during the recent Subcommittees hearing, we do not believe cell culture will shift the production paradigm. In general, we believe the federal government should focus on overall pandemic preparedness, rather than investing solely in a particular technology. The egg-based production method we currently utilize is a technologically sophisticated process that has proven adaptable to emergency situations and it enabled our unprecedented response to the current pandemic. No other technology is proven.

Contrary to popular perception, cell culture technology does not necessarily increase yields and there is no evidence that cell culture derived vaccine is more efficacious than egg-derived vaccine.

Importantly, cell culture shares many of the same inherent limitations as the current egg based technology, as many steps in the process are the same regardless of the technology used. For example, growing antigen on any medium can only begin after the seed virus is isolated and is sent to manufacturers by the FDA. Additionally, no matter which production method is used, all vaccines must undergo rigorous quality control and safety testing. This testing is done for each individual vaccine production lot and accounts for approximately 85 percent of the production timeframe. The testing is comparable for both egg-based and cell culture technologies. In addition, as Dr. Jesse Goodman, FDA Acting Chief Scientist, Deputy Commissioner for Scientific and Medical Programs, pointed out at the hearing, virus yields can also be challenging when using cell culture. The H1N1 yield problem is not unique to egg technology.

The H1N1 influenza pandemic has provided us with an opportunity to directly compare the availability of influenza vaccines produced with egg-based and European cell culture based production. Each of the methods produced clinical lots within similar timeframes. Large-scale production was initiated in nearly the same timeframe. More importantly, the US was the first country to start a nationwide influenza immunization program, receiving all of its vaccine from egg-based production.

The egg-based technology and cell based technologies will co-exist over the next decade and both are necessary to keep capacity at the highest possible levels. If we are to really change the current production paradigm (egg or cell-based), we should be investing in game-changing technologies, such as the so-called "universal influenza vaccines". These types of vaccines, while years away, offer an opportunity to proactively address a pandemic, rather than react to it. The government can best help in the advancement of new production technologies and next generation vaccines by funding and supporting research. Corporations should be responsible for investment in new production facilities, which can only be supported and maintained by market demand.

The government can play a significant role in ensuring the continued investment in influenza vaccine development and production by applying resources to ensure that demand and uptake of the seasonal influenza vaccines in the US keeps up with the growing capacity. By immunizing more individuals with seasonal influenza, we are advocating prevention, preparing for the next pandemic and encouraging manufacturers to continue to invest and stay in the US market.

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DAVID L. LAKEY, M.D.
COMMISSIONER

January 8, 2010

The Honorable John D. Dingell
Chair Emeritus
2328 Rayburn House Office Building
Washington, DC 20515
United States House of Representatives
Washington, DC 20515

Dear Chairman Dingell:

Thank you for the opportunity to present the Texas perspective on H1N1 pandemic response efforts at the joint hearing of the Subcommittee on Health and the Subcommittee on Oversight and Investigations on November 18, 2009. The attached document provides answers to follow-up questions on Texas' response to H1N1 as submitted by Chairman Waxman on December 15, 2009.

Texas is in a position of responding to many disasters each year, from H1N1 to food-borne outbreaks and natural disasters, such as tornados, floods and hurricanes. Consequently, Texas understands how critical it is to maintain state public health capacity to effectively respond to public health threats. This capacity is in part possible due to continued assistance through federal funding provided to all states for Public Health Emergency Preparedness (PHEP) and the Hospital Preparedness Program (HPP).

While the overall H1N1 response efforts have not been perfect, the amount and quality of the work by public health responders at the local, state and national level is commendable. I appreciate your interest in and continued support of public health. If you or your staff have further questions, I can be reached at 512/458-7363.

Sincerely,

David L. Lakey, M.D.
Commissioner

cc: The Honorable Henry Waxman
Earle Green, Chief Clerk

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DAVID L. LAKEY, M.D.
COMMISSIONER

January 8, 2010

1. **Do you believe public providers have been able to adequately respond to their patients' demand for the H1N1 vaccine?**

   No providers, either private or public, were able to adequately respond to their patients demands initially due to the very limited amount of vaccine that was available nationwide. Once vaccine was available to them, public providers performed very well in distributing the vaccine and getting individuals vaccinated.

   Public providers have done well in making H1N1 vaccine available to priority populations both directly and through creative community partnerships. They have conducted a large number of daytime, after-hours and weekend clinics in convenient locations. They have also assisted other community providers to ensure the availability of H1N1 vaccine to priority populations.

   In Texas, to provide a public safety net, local public health departments and public hospitals/clinics were among the first to receive H1N1 vaccine. In response to early concerns among local health departments about the proportion of vaccine they were receiving to serve their communities, DSHS increased its allocation to local health department to 20 percent of the state's allotment each week. Supplies of vaccine have increased over time and are now plentiful across all provider groups in the state.

2. **Do you believe the private sector has been able to adequately respond to their patients' demand for the H1N1 vaccine?**

   As noted above, no sector was able to adequately respond to the demand for vaccine initially due to the very limited supply of vaccine. However, as vaccine became more available to them, the private sector became a very effective tool in the delivery of H1N1 vaccine.

   The Texas Department of State Health Services (DSHS) has a robust partnership with the many private sector providers who registered with the state to receive and administer the H1N1 vaccine. Texas' vaccine allocation strategy has been to first supply H1N1 vaccine to providers who indicated at the time of registration that they would be serving persons in the highest priority populations identified by the CDC. Early on, vaccine allocations to Texas were smaller than expected, and, as a result, some private sector providers serving these priority populations had to wait weeks before receiving significant amounts of H1N1 vaccine. Despite this delay, private sector providers did an outstanding job of rapidly responding to the needs of their priority patients when H1N1vaccine became available to them. Vaccine is now plentiful across the state.

3. Did Texas follow the CDC's recommended guidelines for prioritizing the H1N1 vaccine for high-risk populations?

Texas adhered to CDC's recommendations in allocating H1N1 vaccine to all public and private providers. The challenge was that vaccine supplies were not sufficient initially to make the vaccine available to all priority populations. In October, Texas focused its vaccine supplies on the highest priority groups beginning with children 2-3 years of age and the health care workers that served them. The state then added pregnant women, 4 year olds, children 5-18 years old at high risk of complications, and all health care workers who provide direct patient care. By November 1, Texas expanded to children six months to one year of age and close contacts of infants under six months old. In mid-November, adults at high risk of complications were added. By December 12, the state began opening up vaccination to the general population due to a sufficient supply of vaccine available.

Nearly 12,000 providers registered to receive and administer H1N1 vaccine, and as part of that process, they indicated the number of persons they intended to vaccinate in each of the CDC risk groups. Texas allocated vaccine to these providers based upon the number of persons each provider reported in the high risk categories and the quantities and formulations of the vaccine allocated to the state. When these providers received notification that a quantity of H1N1 vaccine was available for them to order, they were also reminded of the priority groups that were being targeted at the time.

4. Do you believe the federal government has been effective in communicating to the public about the need and availability of the H1N1 vaccine?

Although I believe the federal government did a good job in communicating the need and availability of the H1N1 vaccine, I also believe there were areas that can be improved for future events.

Communicating clearly to the public is important in any disaster response, and a pandemic response effort is no different. Communicating with the public has been a challenge for a number of reasons. Primarily, the overall context of the situation contributed to the challenges. Vaccine development, manufacturing and distribution are complex processes, and not topics that are easily put into lay terms. In addition, other issues, including multiple priority groups, vaccine supply and varying quantities of each vaccine formulation made these communications more complex.

The federal government kept information flowing to the public, the media and their public health partners at the national, state and local level. The CDC held frequent press conferences, and I believe they performed well at these press conferences. Their leadership, likewise, had frequent conference calls with state and local public health leaders so that a similar message could be delivered at the federal, state, and local level.

However, looking back, the expectations communicated about timing and availability of the H1N1 vaccine supply were too ambitious. The delay in manufacturing H1N1 vaccine created a perception that public health efforts were falling short and that H1N1 vaccine

would be in short supply. This perception of a shortage added greatly to public and provider anxiety and generated pressure on public health entities, which were criticized for not aggressively seeking larger H1N1 vaccine allocations for their jurisdictions.

The delay in vaccine availability also necessitated a delay in using media in the form of public service announcements to increase demand. Although very professional announcements were made for TV and radio, they could not be initially used because, at that time, demand for vaccine was already much higher than supply. Once vaccine supply was plentiful, these products were used, but by that time vaccine demand had decreased due to the overall decrease in H1N1 disease.

Additionally, in an effort to show federal progress on H1N1 vaccine distribution, the federal government publicized state level performance metrics on the timeframes for H1N1 vaccine allocation, ordering and shipping to states. Those metrics did not fully take into account any differences in how H1N1 vaccine was being ordered and distributed in each individual state. They also were outdated at the time they were published. Frequently large orders from Texas were not accounted for in these weekly reports. Thus, these metrics led to misperceptions about states' ordering of the allocated H1N1 vaccines and their distribution of those vaccines to providers administering the H1N1 vaccine to priority groups.

Finally, federal initiatives to help people find a location where they could obtain H1N1 vaccine were inconsistent with state vaccination plans and the amount of vaccine available. The goal of the vaccine locator effort made sense in states where the vast majority of H1N1 vaccine was initially being administered through mass vaccination clinics, public health clinics, pharmacies, or community vaccinators. However, the effort did not fit as well in Texas, where private providers, who were receiving relatively smaller doses of vaccine to serve their patients, were a large part of the initial H1N1 vaccination strategy. Posting their contact information and hours-of-operation to a website for the general public to view would have quickly overburdened these providers.

Despite these communication issues, DSHS appreciates the commitment and responsiveness of the CDC, the Office of the Assistant Secretary for Preparedness and Response, and other federal agencies that have worked closely with state and local public health agencies to address this important public health problem. At the federal, state and local levels, DSHS has been in contact via email, phone and conference calls many times per week working to find solutions to difficult issues. The federal agencies involved in these efforts have been very responsive to feedback and issues raised by the states.

5. **Do you believe the states have the necessary resources and personnel to address pandemics like H1N1? If not, what should the federal government be doing to provide these resources?**

No. Some states were almost totally dependent on the federal public health emergency response funding for their response activities, while other states had more resources to contribute to the effort. The reason is that each state differs in how public health functions are organized and funded. Regardless, any states' resources and personnel to respond would not be sufficient without federal support.

Public health emergency preparedness is a shared responsibility of federal, state and local governments. Ultimately, protecting our nation from public health threats starts at the local level. Without the necessary personnel and infrastructure at the local level and in each state, a national response cannot be effective. The federal government can help by: (1) providing funding to support public health capabilities at the state and local level, (2) providing technical expertise to states to support public health preparedness, (3) developing more robust surveillance systems across the nation to identify public health threats early, and (4) supporting the expansion and strengthening of the public health workforce.

As the nation has seen during this pandemic, response to public health threats requires complex and coordinated public health capabilities. These capabilities include epidemiology, disease surveillance/intervention, public health laboratory testing, food-borne illness protection, public health workforce training, health promotion/disease prevention, communication (between jurisdictions and with providers, the general public and the media), and public health data management (electronic birth and death records, disease registries, immunization registries, electronic disease reporting, passive electronic disease surveillance systems, vaccine tracking and stockpile management systems).

A well-trained public health workforce is the cornerstone of preparedness: qualified laboratory scientists are needed to conduct testing and share timely results with federal, state, and local health officials; epidemiologists and health information specialists must develop and run biosurveillance systems to monitor disease rates and warn of bioterror or food-borne disease outbreaks; stockpile managers are required to receive, store, and dispense medical countermeasures; and public health nurses and doctors must vaccinate populations against infectious diseases, such as H1N1 influenza. The public health workforce has decreased significantly in recent years. We must find strategies to increase the number of public health professionals and to enhance training to ensure that our public health workforce remains ready to respond. Without the human resources, disaster response will not be effective.

The critical personnel and infrastructure for addressing public health threats, including pandemics, has not received the necessary investment to build and maintain core public health capabilities. The declining federal commitment to ongoing preparedness funding as well as funding reductions in many states and local jurisdictions due to economic factors have left the public health system more vulnerable. While state and local public health entities are very appreciative of the public health preparedness funding that has flowed to the states during the past eight years, this funding must remain stable to maintain our level of preparedness. These public health preparedness and response funds have been invaluable in planning for and responding to any number of natural or man-made public health disasters, including pandemics. However, this funding has decreased by 27 percent since FY 2005. The public health emergency response funds that have been made available to states for the 2009 H1N1 pandemic have been important to supporting response efforts. However, this funding is one-time and will not sustain our preparedness for the long term. Unstable funding undermines our ability to sustain our level of preparedness to respond to disasters at the state and local level, which leaves our nation more vulnerable to public health threats.

The federal government should continue to invest in core public health capabilities to sustain the necessary resources and personnel to address public health threats, such as the 2009 H1N1 pandemic. A stable funding stream for preparedness at the federal level will allow state and local governments to be more effective in building and sustaining core public health capabilities that allow state and local public health entities to prepare for and respond to disasters in their jurisdictions, while also protecting the nation.

January 4, 2010

"H1N1 Preparedness: An Update of Vaccine Production and Distribution"
Subcommittee on Health and Subcommittee on Oversight and Investigations
House Committee on Energy & Commerce
November 18, 2009

Questions for the Record
Responses from Jeffrey Levi, PhD
Executive Director, Trust for America's Health

The Honorable John Dingell

1. **Do you believe the federal government has been effective in communicating to the public about the need and availability of the H1N1 vaccine?**

A: Overall, communication surrounding the availability of the vaccine has been strong. The federal government was dealing with a moving target, and communication with the public was flexible to deal with a changing situation. It is difficult for us to assess when the Department or CDC was aware of supply problems and when they made state and local health departments aware of the shortage. The lesson learned from this event should be that administration planning should not just be based on a robust supply, but the very real likelihood of shortage.

That said, the underlying problem with communicating about the need for the vaccine, however, is that the outbreak took place amid a climate of growing vaccine hesitancy. The federal government needs to take seriously the rising mistrust and misinformation about the safety and effectiveness of all vaccines. This pandemic exposed many ongoing problems with vaccine communication: parents believing false information about preservatives in vaccines; obstetricians warning their pregnant patients not to get vaccinated; and healthcare workers worried that flu vaccines would actually make them sick. If our frontline workers do not see the importance of vaccines as a means of preventing infections in healthcare settings and keeping the workforce healthy, it is difficult to expect skeptical Americans to listen to the best scientific evidence. Vaccine communication can not just take place when an outbreak occurs or a new vaccine hits the market. CDC and state and local health departments must continuously reach out to the public, especially health care workers and underserved population, to build up trust in the vaccine system.

2. **Do you believe the federal government had the necessary resources and personnel dedicated to managing the H1N1 pandemic?**

A: Emergency funding levels for H1N1 were sufficient, but there also have been many concerns which were not adequately addressed or funded before 2009. In other words, our system is remarkably good at finding resources on an emergency basis, but it fails in providing the ongoing support for our public health infrastructure. There is just so much you can compensate for on an emergency basis. Had we provided that support, we might have needed less new money for H1N1.

Among the components of our public health system that have been neglected include: the need to modernize and strengthen, in a sustained way, much of the public health infrastructure, how best to manage surge capacity during a mass event, and developing a reimbursement system for uncompensated care during an emergency. In addition, prior to this year, policies called for many preparedness functions to be state and local responsibilities without provision of federal support for these needs, including the expectation that states would purchase a significant portion of antiviral medications to protect their own citizens. The federal government has been able to address some of these underlying issues in the short-term as they grapple with the H1N1 pandemic, but longer-term solutions are needed.

3. Do you believe the states have the necessary resources and personnel to address pandemics like H1N1? If not, what should the federal government be doing to provide these resources?

A: No, state funding for public health preparedness, pandemic planning, and public health infrastructure overall has declined over the years. The outbreak took place amid the most severe economic recession in a generation. In TFAH's latest report on public health preparedness, *Ready or Not? 2009*, we found 27 states had cut funding for public health from FY 2007-2008 to FY 2008-2009. Federal public health preparedness funding has also declined 27 percent since FY 2005, and Congress has not appropriated state and local pandemic funding since FY 2006. These overlapping cuts have led to real erosion in capacity on the ground: according to National Association of County and City Health Officials, 15,000 local health jobs have been lost since 2008. Disaster preparedness is especially dependent upon a stable workforce because it relies heavily on training and exercises. Although state and local health departments were grateful for the funding provided in the supplemental, some states were unable to rehire previously laid off workers, while many had to shift employees from other areas to pandemic response.

The best thing Congress could do to support the front lines on public health preparedness would be to provide funding on a predictable, consistent basis, rather than funding by emergency. Before the most recent supplemental appropriations measure, the previous state and local pandemic grants had all been expended as of summer 2008. We continuously hear from health departments that they would rather have a reasonable, predictable funding stream than a huge influx of money that will disappear in a year. As I stated in my written testimony, we do not fund fire departments when a fire breaks out, so it is irresponsible to fund health departments only after a disease outbreak or disaster. The public health investment fund, included in the House health reform bill, would go a long way to addressing this need.

4. Did the state and local health departments have the guidance and resources necessary to manage and distribute the H1N1 vaccine? If not, what resources should the federal government have provided?

A: The federal government did provide comprehensive recommendations for distribution of vaccine and prioritization of populations. A good deal of discretion was left to the states and localities to determine their own specific distribution mechanisms, given their knowledge about the population and infrastructure in each area. However, the planning undertaken by localities was based on the assumption of a robust supply of vaccine. Once the shortage became apparent, the federal government should have provided additional guidance about how to prioritize and distribute vaccine in the most equitable and efficacious manner. The shortage, combined with wide variation in prioritization between regions, led to additional confusion among the American people on top of an already confusing and frightening process. I recommend CDC review the distribution process, including after-action reports from state and local health departments, to determine what additional technical assistance is needed from the federal government before the next outbreak. Pandemic plans at the federal, state and local level must all be updated to include lessons learned from the H1N1 outbreak, and I urge this Committee to conduct oversight of that process.

As for resources, states need a consistent funding stream from the federal government. The federal government should provide this through state and local pandemic preparedness grants, through the Public Health Emergency Preparedness cooperative agreements from CDC, and through overall public health infrastructure funding. Consistent funding would allow states to build a stronger biosurveillance system to detect outbreaks and emerging infections, train a capable workforce, and respond when an emergency occurs.

5. Has the federal government done enough to encourage the production of such vaccines using more advanced vaccine manufacturing technologies such as cell-based or recombinant? If not, what would you recommend the federal government do to encourage the use of such technologies?

A: The investment in pandemic preparedness that began under the Bush Administration has helped the nation take great strides in building domestic vaccine capacity. However, we are still a few years away from the payoff on this investment – especially with regard to new technologies. Thus, for the H1N1 vaccine, we were still reliant on old egg-based production lines. Novartis' U.S. facility to manufacture cell-based flu vaccine opened in December 2009, but will not begin producing licensed vaccine until 2014.

But we are still lagging in a number of areas that could have made a difference in responding to this pandemic. First, development of a "universal" flu vaccine, one that can protect against all variants of the virus is still lagging. Second, we need modernized rapid diagnostics that can tell us more about how the virus is spreading and focus our attention on who needs treatments. And third, we need better antiviral treatments. Those

we have are important, but only modestly effective. One issue holding back American technological advancement is the chronic underinvestment in BARDA, the Biomedical Advance Research and Development Authority. The Center for Biosecurity at University of Pittsburgh Medical Center has recommended an annual appropriation of $1.75 billion for BARDA's research agenda. In the recently passed Labor-HHS appropriations bill, BARDA received $305 million, an increase of $30 million over FY2009 While it was good to see an increased investment in a difficult budget year, the disparity between the recommended amount and actual funding stream illustrates how far we are from giving BARDA the resources to achieve its mission. There is little incentive for pharmaceutical companies to develop new vaccines or drugs for emerging diseases without investment or a guarantee of purchase from the government.