

INFLUENZA: PERSPECTIVE ON CURRENT SEASON AND UPDATE ON PREPAREDNESS

HEARING BEFORE THE SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS OF THE COMMITTEE ON ENERGY AND COMMERCE HOUSE OF REPRESENTATIVES ONE HUNDRED THIRTEENTH CONGRESS

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INFLUENZA: PERSPECTIVE ON CURRENT SEASON AND UPDATE ON PREPAREDNESS

WEDNESDAY, FEBRUARY 13, 2013

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:05 a.m., in room 2123 of the Rayburn House Office Building, Hon. Tim Murphy (chairman of the subcommittee) presiding.

Members present: Representatives Murphy, Burgess, Gingrey, Harper, Olson, Griffith, Johnson, Ellmers, Barton, Upton (ex officio), DeGette, Lujan, Butterfield, Castor, Tonko, and Green.

Staff present: Gary Andres, Staff Director; Matt Bravo, Professional Staff Member; Karen Christian, Chief Counsel, Oversight; Sean Hayes, Counsel, Oversight and Investigations; Sean Hayes, Counsel, Oversight and Investigations; Katie Novaria, Legislative Clerk; Andrew Powaleny, Deputy Press Secretary; Krista Rosenthal, Counsel to Chairman Emeritus; Alan Slobodin, Deputy Chief Counsel, Oversight; John Stone, Counsel, Oversight; Brian Cohen, Democratic Staff Director, Oversight and Investigations, and Senior Policy Advisor; Kiren Gopal, Counsel; Elizabeth Letter, Democratic Assistant Press Secretary; Anne Morris Reid, Democratic Professional Staff Member; and Stephen Salisbury, Democratic Special Assistant.

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

Mr. MURPHY. Good morning, everyone.

Today we convene the first hearing of the Subcommittee on Oversight and Investigations in the 113th Congress. I would like to welcome back the members who served here in the 112th and welcome our new members joining us for 113th. I want to particularly welcome my colleague and my friend, the ranking member, Dianna DeGette of Colorado. I am looking forward to working with you and your team here. And this is the first of many hearings and issues that we will be dealing with in an organized, bipartisan way, and I appreciate the witnesses for coming here today.

Today we are here to examine the current flu season and discuss the lessons that will help us prepare for seasonal influenza and pandemics in the future. This committee has investigated into response efforts during previous sessions, last during the H1N1 pan-

demic in 2009, and oversight of the agencies involved will remain a priority going forward.

I welcome our distinguished witnesses whose agencies play key roles in the federal government's response to influenza. Dr. Thomas Frieden, Director of the Centers for Disease Control and Prevention, welcome here today. Dr. Jesse Goodman, Chief Scientist at the Food and Drug Administration, welcome here, Doctor. And I also thank Marcia Crosse, Director of the Health Care Division at the Government Accountability Office. Welcome here as well, Doctor. The GAO has done a number of reports analyzing federal response to seasonal and pandemic outbreaks.

Well, this year's flu season came a little earlier than expected and it looks as though it will have been unfortunately worse than average. This is particularly true in my home of southwestern Pennsylvania, which has the highest percentage of seniors in the country outside of Florida. In the Pittsburgh region, for one, this year's flu season has been labeled a nightmare at local nursing homes that have taken to restricting visitors and quarantining sick patients. For seniors in southwestern Pennsylvania and across the country, hospitalization rates and deaths have increased sharply. And sadly, this season has also taken its toll on the most vulnerable. Through February 2, there have been 59 pediatric deaths.

Today, I hope to hear how the CDC, FDA, and the vaccine manufacturers are working together through development of new medications, better surveillance to prevent shortages, and increased vaccination to protect the public from deadly flu viruses. Remember, all of us should consider vaccination to not only protect ourselves from getting sick, but also our children, grandparents, coworkers, and neighbors. The CDC recommends annual vaccinations for all persons aged 6 months and older, yet less than 50 percent of Americans actually get immunized. Today, I hope to learn what the biggest barriers are to people getting vaccinated and how can we remove them.

Each year a new vaccine is produced and administered to protect against the strains expected to be most prevalent that year. Because of the increased activity this season, many have wondered about the process that creates this seasonal vaccine and whether it can be improved. Questions have also been raised about vaccine effectiveness. We have heard from government representatives that this year's vaccine has an effectiveness rate of 62 percent, meaning that someone who is vaccinated is 62 percent less likely to see a doctor for the flu than someone who hasn't been vaccinated. To some this might seem low, but we have heard that this is actually within the range of what is expected. How can we improve upon that and what efforts are currently underway in the government and the private sector to ensure that we do?

This year, we have also heard reports of spot shortages of vaccine and certain antiviral treatments. Yet we know that, overall, vaccine and antiviral supply will still exceed demand. What role did the federal government play, along with its public health partners at the State and local level, in responding to these supply issues and what can we learn from these efforts going forward?

Finally, I wish to again thank the ranking member of the Committee, Ms. DeGette. This hearing has been a bipartisan effort, and

the ranking member and I have been working together on a number of issues. I thank her for her support on this and other issues as we move forward. As well, I would also like to thank the witnesses, as I said before, and I had time to meet with representatives from the CDC, and staff also reports to me that all of your agencies have been more than helpful in addressing their concerns, so thank you in preparation for these complex issues.

[The prepared statement of Mr. Murphy follows:]

PREPARED STATEMENT OF HON. TIM MURPHY

Today we convene the first hearing of the Subcommittee on Oversight and Investigations in the 113th Congress. I'd like to welcome back the members who served here in the 112th and welcome our new members joining us for 113th.

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I welcome our distinguished witnesses whose agencies play key roles in the federal government's response to influenza: Dr. Thomas Frieden, Director of the Centers for Disease Control and Prevention, and Dr. Jesse Goodman, Chief Scientist at the Food and Drug Administration. I also thank Marcia Crosse, Director of the Health Care Division at the Government Accountability Office, for being here. The GAO has done a number of reports analyzing federal response to seasonal and pandemic outbreaks.

This year's flu season came a little earlier than expected and it looks as though it will have been worse than average. This is particularly true in Southwestern Pennsylvania, which has the highest percentage of seniors in the country outside of Florida. In the Pittsburgh region, this year's flu season has been labeled a "nightmare" at local nursing homes that have taken to restricting visitors and quarantining sick patients. For seniors in Southwestern Pennsylvania and across the country, hospitalization rates and deaths have increased sharply.

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Finally, I wish to thank the Ranking Member of the Committee, Ms. DeGette. This hearing has been a bipartisan effort and the ranking member and I have been working together on a number of issues. I thank her for her support. As well, I would also like to thank the witnesses: I have had time to meet with representatives from the CDC, and staff also reports to me that all of your agencies have been more than helpful in addressing these complex issues.

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Mr. MURPHY. With that, I will now recognize Ranking Member Ms. DeGette for her opening statement for 5 minutes.

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

Ms. DEGETTE. Thank you very much, Mr. Chairman, and welcome, Mr. Chairman. We are delighted to have you. And the chairman is correct. We have been working quite closely together ever since his appointment on issues that are facing this committee, and given the Energy and Commerce's broad jurisdiction, really, the world is our jurisdiction on this subcommittee. Mr. Dingell and I think even Mr. Barton would agree, this is probably one of the most venerable and important committees in the U.S. House of Representatives, and I look forward to working very hard with you, Mr. Chairman, and the rest of the committee to making sure that we have very thorough and important investigative hearings.

Flu preparedness is one of those issues. This committee has had a number of hearings over the years on preparedness, not just for the next flu season but also in the event, which we hope will never happen, of a pandemic, and I am glad that you have scheduled this first oversight hearing on this issue because it is one that the committee has had concern about for many years. According to the CDC, this was a bad flu season. The worst of it is now nearing its end, and fortunately, this flu season did not reach pandemic proportions.

If you can find good news in this flu season, it has been a good demonstration of the public health system operating as it should. The FDA worked closely with manufacturers to ensure adequate vaccine supply, and the CDC collaborated with the States in its surveillance and tracking efforts. When the season peaked in January, CDC got the word out and many people who had delayed were still able to get vaccinated. Now, while we saw spot shortages of vaccine and antiviral drugs in certain areas of the country, unlike previous seasons, we didn't have any serious shortages. But I must say, the threat of influenza is one that we cannot underestimate, given its potential impact on the Nation and the world's public health, security and economy.

Vaccination rates are one area in particular where we can make significant progress. The latest data from November shows that only 36.5 percent above those who are 6 months old got vaccinated. The most important step in protecting against the flu is to get a flu shot, so I am interested in hearing from the witnesses how we can improve our vaccination rates. The Affordable Care Act is going to be one way to improve flu prevention and care. Because of this Act, 54 million Americans can now receive a free flu shot through their private health care plan, and next year CBO estimates that 14 million Americans who would otherwise be uninsured will instead have health care coverage. That number will increase to 27 million by 2017.

Each flu season is a practice run for how well we would do in a pandemic. After the H1N1 pandemic in 2009, it became really ap-

parent that we would need more vaccine alternatives to deal with potential shortages. We need to be able to make vaccines faster and to make them more effective against the flu, and that is why I am excited to see that the FDA has approved numerous alternative vaccine technologies that hold the potential for faster startup of the manufacturing process in the event of a pandemic. These new approvals provide alternatives to our current decades-old use of time-intensive egg-based technology to produce vaccines. In the event of a pandemic, egg-based production would be too slow to meet heightened demand for vaccine with the potential loss of millions of lives around the world. In November, the FDA approved the first seasonal flu vaccine using cell-based technology. With cell-based technology, the virus strains are grown in animal cells instead of eggs. This is a huge step forward in expanding vaccine supply. And last February, FDA approved FluMist, the first vaccine to protect against four rather than three strains of the flu. By improving protection against the flu, these new quadrivalent vaccines will protect millions of Americans.

So Mr. Chairman, these are great examples of laudable government investment, but beginning in 2005, HHS recognized a gap in the public health system and subsequently made investments to deal with this, and that is truly a government success story. While I am encouraged by the fact that these alternative technologies have come to fruition, we have a long way to go. We must remain vigilant against the risks of a flu pandemic. Pandemics are infrequent, highly unpredictable and come on suddenly, and so we have to have constant vigilance. I appreciate our witnesses coming here today. I am eager to hear what they have to say about the progress that we have made and the state of vaccine innovations and improvements because, frankly, we must do whatever we can to make sure that we have better flu preparedness.

Thank you, and I yield back.

Mr. MURPHY. I appreciate the gentlelady's comments, and I now recognize the chairman of the full committee, the gentleman from Michigan, Mr. Upton.

OPENING STATEMENT OF HON. FRED UPTON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MICHIGAN

Mr. UPTON. Well, thank you, Mr. Chairman, and welcome you to your first chairmanship of the Oversight Subcommittee here in the big House. I want to welcome you to that.

I had the opportunity, as you know, to chair this subcommittee a number of years ago, so I know firsthand the important work that can be done from that post. Oversight has a number of very, very important purposes, but one of the most significant is ensuring that our federal programs are working properly and efficiently, especially in matters relating to public health and safety. It is often a bipartisan role, and I appreciate the role that your ranking member has well, Ms. DeGette.

With regard to the flu, this committee examined the response to the H1N1 pandemic 3 years ago and had probed influenza vaccine shortages in 2004. We have a tradition of doing strong oversight in this area and we are well aware that this has been a very tough flu season and we have been especially troubled by this season's

particularly harmful impact on the elderly and some kids too. We have also heard reports of spot shortages, especially in hard hit areas, and questions about the effectiveness of this year's vaccine.

The good news is that while outbreaks appear to be on the decline overall, parts of the country are experiencing increases, so it remains important to hear the most up-to-date facts and figures on the current season and examine what the government is doing to prepare for future seasons as well as pandemics.

Personally, some of what I have heard from my neighbors in Michigan about this year's flu is similar to what we have seen in the national press. Lakeland Healthcare, which provides care in my hometown, reported to my office that while they did not have a shortage of vaccine, they had to help supplement their supplies with other health care providers. I am pleased whenever I hear that providers are communicating with each other to address these issues at the local level, but remain concerned about whether there is enough supplies available in the next outbreak.

While we are still evaluating the responses to the flu season, we need to be prepared for the possibility of a worse outbreak or even a pandemic in the future. I am excited about the recent innovations in vaccine technology and the role they play, and I welcome our witnesses and I yield the balance of my time to Dr. Burgess.

[The prepared statement of Mr. Upton follows:]

PREPARED STATEMENT OF HON. FRED UPTON

I would like to welcome you to your first hearing as Chairman of the Oversight and Investigations Subcommittee.

I had the opportunity to chair this subcommittee a number of years ago, so I know firsthand the important work that can be done from this post. Oversight has a number of important purposes, but one of the most significant is ensuring our federal programs are working properly and efficiently, especially in matters relating to the public's health and safety.

With regard to influenza, this committee examined the response to the H1N1 pandemic three years ago and probed influenza vaccine shortages in 2004. We have a tradition of doing strong oversight in this area. We are all aware that this has been a tough flu season and we have been especially troubled by this season's particularly harmful impact on the elderly and some children. We've also heard reports of spot shortages, especially in hard hit areas, and questions about the effectiveness of this year's vaccine. The good news is that while outbreaks appear to be on decline overall, parts of the country are experiencing increases, so it remains important to hear the most up-to-date facts and figures on the current season and examine what the government is doing to prepare for future seasons as well as pandemics.

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While we are still evaluating the response to this flu season, we need to be prepared for the possibility of a worse outbreak or even a pandemic in the future. I am excited to hear about recent innovations in vaccine technology and the role they will play in these efforts. I welcome Dr. Frieden of the CDC, Dr. Goodman of FDA, and Marcia Crosse of the GAO, and look forward to their testimony.

Thank you again to the witnesses for joining us today, and again congratulations and good luck to our new Oversight and Investigations Chairman.

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

Mr. BURGESS. I thank the chairman for the recognition. I thank our witnesses for being here today. We have heard already that this flu season was one of the worst that the United States has experienced in several years. It began early and was particularly harsh. It is most often thought to affect infants and the elderly, but as we saw many times in this outbreak, all age groups are susceptible to infection and the implications of a flu infection.

Talking about the statistics is one thing but I will tell you from firsthand experience, when you lose a vibrant 17 year old, a member of the golf team from one of your high schools in your hometown over the Christmas holidays, it has a profound effect on the entire community. Max Schwolert was that individual from Flower Mound, Texas. He actually became ill while on holiday with his family up in Wisconsin and Minnesota but ultimately succumbed. He became ill at Christmas and succumbed by December 29 to a staph infection that was superimposed on his influenza. His dad is a youth minister at Faith Lutheran Church and obviously a very high-visibility family within the community and certainly took its toll on members of the community. They have done good work since that time in encouraging vaccination, and as we have already heard this morning, the vaccination was available this year, was perhaps a little bit better, so thank you for your efforts on that to develop a better vaccine. It doesn't protect everyone in every instance but it certainly improves the odds, and as we saw in this unfortunate case, being young and healthy does not always confer the immunity that we think it should.

We have got a lot to learn yet about the future of vaccination, and while I recall the enthusiasm of the cell-based cultures in 2005 and the enthusiasm for finding a vaccine that didn't have to be changed every year, we are now 7 years, 8 years later and I do have some questions about when those things will be coming online.

The flu season is almost done, not quite done. The overall effectiveness of the vaccine this year was good to better than we might have expected and preparedness was something that certainly is laudable, so I am grateful to all our witnesses for being here today. We do have a big task ahead of us and we need to keep vigilant, and I will yield back.

Mr. MURPHY. I thank the gentleman from Texas.

I would now like to introduce the witnesses testifying today. First, Dr. Thomas Frieden, the Director of the Center for Disease Control and Prevention. Dr. Frieden was appointed in 2009 and also serves as the Administrator for the Agency of Toxic Substances and Disease Registry. Dr. Jesse Goodman is the Chief Scientist for the Food and Drug Administration. Dr. Goodman has served in that position since 2009 and has previously testified before the subcommittee on influenza preparedness. Thank you. And Marcia Crosse. Dr. Marcia Crosse is Director of the Government Accountability Office Health Care Team. Dr. Crosse is responsible

for overseeing GAO evaluations in the area of biomedical research, bioterrorism, disease surveillance and other health issues.

You are all aware that the committee is holding an investigative hearing, and when doing so has the practice of taking testimony under oath. Do you have any objections to testifying under oath, any of you? Seeing no objections, the Chair then advises you that under the rules of the House and the rules of the committee, you are entitled to be advised by counsel. Do you desire to be advised by counsel during your testimony today? The panel answers no. As chairman, I say that case, please rise and raise your right hand and I will swear you in.

[Witnesses sworn.]

Mr. MURPHY. You are now under oath and subject to the penalties set forth in Title XVIII, section 1001 of the United States Code. You may now give a 5-minute summary of your written statement. So we will start off with Dr. Frieden. Dr. Frieden, you are recognized for 5 minutes.

TESTIMONY OF THOMAS FRIEDEN, M.D., M.P.H., DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION, DEPARTMENT OF HEALTH AND HUMAN SERVICES; JESSE L. GOODMAN, M.D., M.P.H., CHIEF SCIENTIST, FOOD AND DRUG ADMINISTRATION; DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND MARCIA CROSSE, PH.D., DIRECTOR, HEALTH CARE, GOVERNMENT ACCOUNTABILITY OFFICE

TESTIMONY OF THOMAS FRIEDEN

Dr. FRIEDEN. Thank you very much, Mr. Chairman and members of the subcommittee. I am Dr. Tom Frieden, Director of the Centers for Disease Control and Prevention, and I appreciate this opportunity to share with you the latest information about influenza.

I think there are four basic bottom-line issues here. First, flu is a deadly and costly disease. Second, this year's season has been worse than average and particularly severe for the elderly. Third, we are making progress applying the best tools, vaccine and treatment that we have, but fourth, we still do need better tools and we are making some progress in that area.

Every year in the United States on average, between 5 and 20 percent of all Americans get influenza. That results in tens of millions of cases, more than 200,000 hospitalizations, more than \$10 billion in direct medical costs, and over \$80 billion in societal costs including an estimated \$17 billion lost work days, many of which could be prevented by vaccination.

Flu seasons are unpredictable and they can be severe. We estimate that in recent decades, between 3,000 and 49,000 people have died each year from influenza. The 1918 pandemic killed more than 50 million people around the world, and of all of the infectious diseases that occur in nature, influenza remains the one that results in those of us who work in public health losing the most sleep.

This year's flu season began early, and for most of the country the 2012-2013 season has already peaked and begun to decline, but there are still many cases around the country, and it is likely that flu activity will continue for several weeks.

I would like to just show a series of slides that shows the spread of influenza through the country. You can see it emerging in the South, Southeast, spreading throughout the country until virtually the entire country was seeing relatively high rates. So we have seen a relatively hard-hitting flu season this year. The predominant virus is H3N2, which tends to cause more severe illness among the elderly, and the next slide shows the hospitalization rate among the elderly, and what you can see is that it is about twice as high this year as in previous years, and this is for laboratory-confirmed influenza hospitalization.

Although it is far from perfect, flu vaccination is by far the best tool we have to fight the flu. Unfortunately, it is not as effective as we would like and is less effective for the elderly, particularly the frail elderly. Vaccination of health care workers and children not only protects these individuals but also appears to benefit the community. Despite some spot shortages late in the season, there was a good supply of vaccine this year with about 145 million doses and about 40 percent uptake. Individuals who have underlying health conditions only had a 42 percent flu vaccination rate, so we really need to do better for particularly the higher-risk populations.

We can all reduce flu by staying home when we have a cough and covering coughs and sneezes and, importantly, for people who are under 2 or over 65 or have underlying conditions, getting seen promptly and treated can reduce the severity of influenza.

Flu is also a great example of global collaboration. A hundred and ten countries track the spread of flu, and we have staff around the world who work with countries because if they identify it sooner, it helps us to identify what we should put in the vaccine and what we can do to reduce the burden of flu here. We have a unique role in monitoring and providing recommendations and guidance and supporting State and other partners but we also work very closely with other federal agencies including FDA, NIH, and BARDA to ensure an adequate and safe supply of vaccine.

There is a great example of collaboration between federal, State and local levels through the 317 and VFC programs and with the private sector for manufacturing, distribution, treatment with health care systems that protect their patients by increasing health care worker vaccination.

Looking to the future, I think we can see improvements in technology. In manufacturing, some progress is being made. FDA, BARDA, NIH and private manufacturers are coming up with new products. You could describe these as important and useful tweaks but yet no breakthroughs in terms of a better, longer lasting, more effective vaccine. One of the tweaks has been a potency assayed to speed up the process of producing flu by about a month through work of CDC scientists that is now being validated in collaboration with the FDA. We have also increasingly been unleashing the genomic revolution to come up with faster growing and more effective strains that we provide to the manufacturers. We are also looking at the next generation of diagnostics that use the genomic revolution again to identify strains more rapidly.

Flu emphasizes that we are all connected by the air we breathe, and the emergence or spread of flu anywhere in the world is a potential risk anywhere else in the world. In conclusion, there is light

at the end of this year's flu season tunnel but many are still at risk. At this point prompt treatment of those at high risk is key to reducing illness and death. We are already tracking flu strains in the southern hemisphere as we head toward developing a vaccine for next year's flu season, and we continue to build on our global capacity to find and stop new pandemic threats where and when they emerge rather than waiting for them to reach our shores.

Thank you, and I look forward to answering your questions.
[The prepared statement of Dr. Frieden follows:]



**Testimony before the
Committee on Energy and Commerce
Subcommittee on Oversight and
Investigations
United States House of Representatives**

**Influenza: Perspective on Current Season and
Update on Preparedness**

Thomas R. Frieden, M.D. M.P.H.

**Director, Centers for Disease Control and Prevention and
Administrator, Agency for Toxic Substances and Disease
Registry
U.S. Department of Health and Human Services**



**For Release upon Delivery
Wednesday, February 13, 2013
Expected at 10:00 a.m.**

Good morning Mr. Chairman, Members of the Committee. I am Dr. Tom Frieden, Director of the Centers for Disease Control and Prevention (CDC). CDC works 24-7 to save lives and protect people from harm. Tragic and often preventable hospitalizations and deaths each year from seasonal influenza remind us that seasonal influenza epidemics are a significant public health burden. I'm happy to be with you today to discuss this season's epidemic, and to illustrate public health action to identify serious health problems and to coordinate targeted responses that protect our Nation and its citizens from public health threats, saving both lives and money.

In my testimony today, I will provide an overview of current flu activity, how we monitor the flu, and factors associated with flu vaccine supply, effectiveness, and uptake. But first let me provide you with a general overview of seasonal influenza.

- Influenza (the flu) is a contagious respiratory illness caused by influenza viruses. It can cause mild to severe illness, and at times can lead to death. Some people, such as older people, young children, and people with certain health conditions, are at higher risk for serious flu complications.
- In the United States each year, on average, 5 percent to 20 percent of the population get the flu, causing more than 200,000 hospitalizations and more than \$10 billion in direct medical costs for hospitalizations and outpatient visits from seasonal flu-related complications.
- Flu seasons are unpredictable and can be severe. Over a period of 30 years, between 1976 and 2006, estimates of flu-associated deaths in the United States ranged from a low of about 3,000 to a high of about 49,000 people.
- This year's flu season began relatively early compared to recent seasons, with elevated flu activity across most of the United States. For most of the country, the 2012-2013 season has peaked and begun to decline, but there are still many cases and it's likely that flu activity will continue for several more weeks.
- The timing, geographic spread, and severity of flu season are unpredictable. The predominant circulating flu virus this year is H3N2, which tends to cause more severe illness, particularly among the elderly.
- Although it is far from perfect, annual flu vaccination is, by far, the best tool to prevent influenza. There are other important steps that we can all take, including following simple guidelines to reduce transmission including staying home when you are sick and covering coughs and sneezes.
- There was a robust supply of vaccine this year, and we understand that despite spot shortages there is still vaccine available. We continue to recommend that people of all ages be vaccinated.
- Importantly, people who believe they have the flu if they are very young, elderly, or have underlying conditions should see their doctor early as antiviral medications can help shorten the length of illness and avoid more serious outcomes.

Introduction

CDC provides the cutting-edge scientific and programmatic foundation and leadership for the diagnosis, prevention, and control of influenza domestically and internationally. Our annual flu efforts help us be better prepared by strengthening our surveillance and diagnostic capacity; improving public awareness and provider knowledge about influenza and the importance of vaccination, other prevention measures, and early treatment; and enhancing our international, Federal, State, and local partnerships to respond quickly to influenza epidemics. The tracking and control of influenza requires – and is a great example of – excellent international cooperation.

We regularly review and adopt recommendations of the Advisory Committee on Immunization Practices (ACIP) for all vaccines licensed for use in the United States including annual influenza vaccination. Nationally, CDC tracks the distribution and availability of vaccine doses as reported to CDC by influenza vaccine manufacturers, and provides vaccine for publicly-funded vaccine programs. Additionally, CDC's health communications experts ensure that the public has easy access to timely information about the flu, ways to prevent the spread of disease, and information about treating the flu. CDC prepares materials and messages aimed at various audiences (e.g. the general public, healthcare providers, parents, older adults) to share information about protecting the population from influenza. Next, I will provide you with a current update of seasonal influenza activity, and then discuss in more detail how CDC works to protect Americans from influenza each year.

Current Influenza Activity

The 2012-2013 influenza season began relatively early compared to recent seasons and by February 5th, 2013, flu activity was high across most of the United States. It is not possible to predict when this season will peak or how severe it will be, but based on past experience, it's likely that flu activity will continue for several more weeks to come. According to CDC's latest FluView report, influenza activity remains elevated overall with activity decreasing in some parts of the country, but increasing in others. In particular, flu activity has been declining in the east and increasing in the western part of the country. Key indicators reflecting severity, such as hospitalizations and deaths, remain significantly elevated, with the greatest impact occurring among people 65 and older.

For the week of January 27-February 5, the proportion of people seeing their health care provider for influenza-like illness (ILI) decreased but remains above the national baseline. Since October 1, 2012, 7,224 laboratory-confirmed influenza-associated hospitalizations have been reported. This translates to a rate of 25.9 influenza-associated hospitalizations per 100,000 people in the United States. In general, hospitalization rates seem to be leveling off and the proportion of deaths attributed to pneumonia and influenza (P&I) decreased. However, the number of deaths reported is still well above the epidemic threshold. Levels of hospitalization and death remain high especially among people 65 years and older, who account for more than half of all reported hospitalizations.

Fourteen influenza-related pediatric deaths were reported during the week of January 27-February 5, 2013. This brings the total number of influenza-associated pediatric deaths reported to CDC for the 2012-2013 season to 59. Since the 2004-2005 season, an average of 78 pediatric deaths occur each season, excluding the 2009 pandemic season for which 282 deaths were reported.

Since October 1st, 2012, CDC has tested 1,358 influenza virus samples for resistance to neuraminidase inhibitors this season like the antiviral drugs oseltamivir (brand name Tamiflu) and zanamivir. Virtually all of the tested viruses are susceptible to these antiviral drugs.

Influenza Surveillance

The information I just shared with you about this flu season in the United States comes to us from a broad network of health care providers and researchers across the country. State and local public health departments are vital partners in domestic influenza surveillance and prevention. We also work closely with our colleagues in other components of the Department of Health and Human Services (HHS) and in the U.S. Department of Defense (DoD), the U.S. Department of Agriculture (USDA), the Department of Homeland Security (DHS), the U.S. Department of State (DOS), the World Health Organization (WHO), and Ministries of Health around the world to conduct and support influenza surveillance. These efforts allow us to monitor the impact of influenza and guide decisions about the vaccine viruses that are recommended for inclusion in influenza vaccines. We also continually test the susceptibility of influenza viruses to antiviral medications and provide recommendations to clinicians for use of these medications.

To improve influenza surveillance, we develop influenza diagnostic tests and provide training to improve influenza testing capabilities at home and abroad. CDC distributes influenza diagnostic testing reagents and supplies to public health partners in the United States and globally. Other CDC efforts include enhancing the use of existing surveillance data, identifying alternative data sources to monitor influenza geographic spread and severity, and classifying which high risk groups are most seriously affected by influenza. CDC conducts state-of-the-art applied research to better understand the properties of influenza viruses, which could provide insight into influenza virus evolution, transmissibility, pathogenicity, and susceptibility to antiviral drugs, as well as the immune response to the viruses. This improved understanding of the antigenic and genetic properties of influenza viruses can lead to the development of better tools to prevent and control influenza.

CDC conducts surveillance for human infections with influenza viruses of animal origin (also referred to as "novel influenza A virus infections"). As I previously noted, the dominant strain this year is H3N2, and not a novel influenza A virus. However, we continue our research and preparedness work because we know that influenza viruses have a propensity to change unpredictably over time, and in rare circumstances a new influenza virus that did not previously circulate in humans can jump the host species barrier from an animal reservoir to humans. Both gradual changes in the virus genome and introduction of a new virus not previously circulating in humans can allow influenza to evade our vaccines and antiviral medications. Working with our partners, we are developing methods to improve

rapid identification and reporting of novel influenza A viruses and new human seasonal influenza virus variants. Alongside our colleagues at USDA, we also conduct research at the animal-human interface to assess the risk of human infection with novel influenza A viruses. Using this information, we evaluate ways to prevent transmission of animal viruses to humans.

Finally, we are exploring the extent to which “next-generation” genetic sequencing technologies can allow us to improve our surveillance of influenza. Advanced molecular techniques will enhance our ability to diagnose infectious diseases, investigate and control outbreaks, understand transmission patterns, determine antimicrobial resistance, and develop and target vaccines (which I will describe below). The work we are pursuing today can allow us to achieve these ends with increased timeliness and accuracy and decreased costs, and will help us detect and manage flu outbreaks in the future.

Vaccine Virus Strain Selection

The best tool we have for the prevention and control of influenza is influenza vaccine. We recommend yearly influenza vaccination. There are several reasons for this. Influenza viruses change over time and we often need to update the vaccine for a new season. Additionally, an individual’s immune response to vaccination can decline over time, necessitating annual vaccination. The influenza viruses selected for inclusion in the seasonal flu vaccines for the northern hemisphere are updated each year based on information about the circulating influenza viruses, influenza activity throughout the world, and how well the previous season’s vaccine viruses might protect against changes in the circulating viruses that are newly identified. There are currently 140 national influenza centers in 110 countries conducting surveillance for influenza viruses and disease activity and CDC is part of this global network. CDC assigns staff in strategic locations to help countries such as Vietnam, Laos, Cambodia, China, India and South Africa to develop their own capacity to monitor influenza – this protects both the people of these countries and people in the US.

The annual WHO vaccine virus decision meetings include representatives from the WHO Collaborating Centers, including the U.S. Collaborating Center for Influenza at CDC, Essential Regulatory Laboratories, including the FDA, and others from WHO’s Global Influenza Surveillance and Response System (GISRS). After WHO makes its recommendations, our colleagues at the U.S. Food and Drug Administration (FDA) Vaccines and Related Biological Products Advisory Committee (VRBPAC) meet to concur with or modify WHO’s recommendation for the United States.

The 2012-2013 seasonal flu vaccine is a trivalent vaccine (a three-component vaccine) with each component selected to protect against a main group of influenza viruses circulating in humans. This year’s vaccine includes two influenza A viruses and one influenza B virus. Two of the three components in the trivalent vaccine for 2012-2013 were changed from the strains included in the 2011-2012 vaccine based on changes in the genomes of influenza viruses, their antigenic profiles and global influenza epidemiology. These changes in the composition of influenza vaccines were based, in part, on CDC’s successful efforts to identify new influenza variants, to rapidly sequence the viral genomes and to provide candidate vaccine viruses to partners in industry.

Vaccine Effectiveness

Choosing the right vaccine strains is key because the closer the corresponding viruses in the vaccine are to the constantly evolving influenza viruses that are currently circulating, the more protective influenza vaccination is. Vaccine effectiveness – or VE – is measured through observational studies (rather than through randomized control trials). In observational studies the study participants make their own decisions about whether or not to be vaccinated. VE is measured by comparing the frequency of influenza illness in the vaccinated and unvaccinated groups, and is usually adjusted for factors (such as presence of chronic medical conditions) that may vary between the groups. Effectiveness represents the percentage reduction in the frequency of influenza illness among people vaccinated compared with the frequency among those who were not vaccinated, assuming that the vaccine is the cause of this reduction.

Estimates of influenza vaccine effectiveness are affected by several factors, including study biases (e.g., confounding bias, selection bias and information bias), the match between the vaccine influenza strains and the circulating strains, host factors and the sample size of a specific study. Specificity of the outcome measured in a study has an important influence on the observed effectiveness. As more data are collected globally from annual studies that estimate effectiveness for RT-Polymerase Chain Reaction confirmed influenza, it is expected that our estimates will become more refined. However, vaccine effectiveness will always vary from season to season, based upon the degree of similarity between the viruses in the vaccine and those in circulation, as well as other factors. In years when the vaccine strains are not well-matched to circulating strains, vaccine effectiveness is generally lower. This year the vaccine has proven to be well-matched to the circulating strains.

In addition, host factors also affect vaccine effectiveness. In general, influenza vaccines are less effective among people with chronic medical conditions and among people age 65 and older, as compared to healthy young adults and adolescents. Because of lower VE that is observed in older adults and people with chronic health conditions, our communications team works to specifically emphasize the importance of early treatment with antiviral medications and vaccination of those people close to these individuals in messages to the public and health care providers.

Each season since 2004-2005, CDC has estimated the effectiveness of seasonal influenza vaccines to prevent influenza-associated, medically attended acute respiratory infection (ARI). The early onset of the 2012-2013 influenza season offered an opportunity to provide early VE estimates this season. These estimates were published in the Morbidity and Mortality Weekly Report (MMWR) on January 11, 2013 and are available on our website (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm62e0111a1.htm>). Initial estimates may be higher than final estimates, however, final VE information will not be known until the end of the season.

The overall vaccine effectiveness estimate of seasonal influenza vaccine for preventing laboratory-confirmed influenza virus infection was 62 percent, roughly the same level of effectiveness as we

experienced in other seasons. (95 percent confidence interval [CI] = 51-71 percent). **Getting a vaccination this year reduced a person's risk of influenza-associated medical visits by approximately 60 percent.** Influenza vaccination with this level of moderate effectiveness offers substantial benefits to the population. Benefits include reducing illness, antibiotic use, doctor visits, time lost from work, hospitalizations, and deaths. We recommend that all Americans over the age of 6 months get vaccinated. Generally the vaccine is much more effective in older children and young adults and less effective in people over the age of 65. CDC will continue to monitor VE throughout the season and provide updates as soon as data become available.

Though these early estimates reinforce the importance of influenza vaccination, they also indicate that some vaccinated persons will become infected with influenza despite having been vaccinated. This does not mean that everyone with influenza-like-symptoms of cough and fever has influenza. There are many other respiratory viruses circulating right now besides influenza. However, we know that some people who get vaccinated will still get infected by influenza. There are a few reasons this may occur. One is that they may be exposed to an influenza virus shortly before getting vaccinated or during the two-week period that it takes the body to gain protection post-vaccination. Another possibility is that a person may be exposed to an influenza virus that is not included in the seasonal flu vaccine; and perhaps some people get it on time with the right strain but don't have sufficient immunity anyway. And, even if well matched, the influenza vaccine is far from perfect, so people can still get infected by and sick from a strain of influenza that is included in the vaccine. While influenza vaccination is not a perfect tool, it is still the best thing we have at our disposal to prevent influenza and we strongly recommend annual vaccination.

Our VE estimates emphasize how critical it is that our continued investment in making better influenza vaccines continues. CDC works to support critical efforts both by HHS's Office of the Assistant Secretary for Preparedness and Response's (ASPR) Biomedical Advanced Research and Development Authority (BARDA), the National Institutes of Health (NIH), the FDA, vaccine manufacturers and others to make faster growing, more effective vaccines. These partners are pursuing multiple strategies to increase the efficacy of the current seasonal flu vaccine and to develop a universal flu vaccine that would provide broader, longer protection against multiple strains or subtypes of influenza.

As an example of one step to improve the range of viruses covered by the influenza vaccine, in 2012, our colleagues at the FDA approved a quadrivalent vaccine with four components rather than three. Though that vaccine was not available this season, we expect it to be available next season.

Vaccine Safety

CDC, in partnership with FDA, leads the Nation's public health effort to provide a safe, effective vaccine supply for all licensed vaccines approved for use in the US. CDC uses multiple systems to monitor vaccine safety including the Vaccine Adverse Event Reporting System (VAERS), the Vaccine Safety Datalink (VSD), and the Clinical Immunization Safety Assessment (CISA).

Over the years, hundreds of millions of Americans have safely received seasonal influenza vaccines. Each year, CDC conducts studies to assess the safety of the annual influenza vaccine. These data are presented in public meetings of Federal advisory committees and published in the peer review literature, providing transparency of the monitoring, research and safety findings. Monitoring to date indicates that this season's influenza vaccine is as safe as past seasonal flu vaccines, and CDC will continue to collaborate with FDA and other HHS agencies and advisory committees to monitor the safety of seasonal influenza vaccine.

Implementing the Annual Influenza Vaccine Program

As of February 1, 2013, 134.6 million doses of flu vaccine had been distributed in the United States of the approximately 145 million doses produced for the 2012-2013 season. The remaining doses will continue to be distributed based on demand.

Our work at CDC extends beyond laboratory and vaccine development work to implementation of seasonal influenza vaccine programs and other clinical interventions. Influenza vaccine is primarily purchased and distributed through the private sector; public sector purchase and distribution account for a small part of the U.S. vaccine supply. A total of approximately 17.9 million doses of 2012-13 influenza vaccine for children and 910,000 doses for adults were purchased using Federal and State funds; this represents about 13 percent of the total U.S. influenza vaccine supply.

At this point in the 2012-2013 influenza season, some vaccine providers have exhausted their vaccine supplies while others have remaining supplies of vaccine. The increased demand for vaccine in some communities has made it more challenging for some people seeking vaccination to locate vaccine. In light of these challenges, CDC is working with state immunization programs to implement strategies that make the best possible use of available influenza vaccines. These include guidance for finding available flu vaccine for purchase and local options for vaccine redistribution.

Vaccination Coverage

During the 2011-12 season, 52 percent of Americans age 6 months and over were vaccinated. Early season 2012-13 coverage was 36.5 percent, which is similar to early season influenza coverage estimates during the 2011-12 season. As of mid-November, more than 60 percent of Americans had not taken advantage of flu vaccination and the protection it offers from influenza and its complications. CDC is working with provider organizations to encourage all providers to recommend a flu vaccination to all their patients and make plans to vaccinate their patients and staff, as well as get vaccinated themselves. Influenza vaccination among health care personnel (HCP) has increased slowly over the past decade, and reached 63.5 percent in the 2010-2011 influenza season; however, coverage is still well below the Healthy People 2020 target of 90 percent. Early-season 2012-13 flu vaccination coverage among HCP was similar to coverage from the same time the previous season. By occupation, flu vaccination was highest among pharmacists (88.7 percent), physicians (83.8 percent), nurses (81.5 percent), and nurse practitioners/physician assistants (73.3 percent). Flu vaccination was lowest among assistants or aides

(43.4 percent) and administrative/non-clinical support staff (54.5 percent). Flu vaccination coverage was highest among HCP working in hospitals (83.4 percent) and lowest among HCP working in long-term care facilities (48.7 percent). CDC is working with partners to educate HCP, especially assistants or aides and non-clinical staff, and HCP working in long-term care facilities about the importance, effectiveness, and safety of annual flu vaccination may increase overall vaccination coverage. Influenza vaccination coverage among HCP is important for patient safety, and CDC recommends that health care facilities should make vaccine readily accessible to all HCP as part of a comprehensive infection control program.

During the 2010-11 flu season, vaccination coverage among pregnant women was 47 percent, which is below the Healthy People 2020 target of 80 percent for pregnant women. By early season 2012-13, flu vaccination coverage among pregnant women was 47.3 percent; this was similar to vaccination coverage from the same time the previous season. Women receiving a health care professional's recommendation and offer were more likely to be vaccinated than those not receiving a recommendation or offer. CDC is working with health care providers for pregnant women, especially obstetricians and midwives, to recommend and offer flu shots to pregnant women throughout the influenza season.

Vaccine Supply Information from National Influenza Vaccine Summit Survey

A brief survey was done by the National Influenza Vaccine Summit, a 300-member partnership, on January 10-18, 2013. The NIVS includes manufacturers, distributors, health departments, provider groups, including pharmacists and medical groups among other influenza immunization stakeholders. Results from 493 survey responses received indicated that there were many doses of vaccine still available, although some immunizers and distributors have exhausted their supplies. More specifically, 10,343,412 doses were reported as in-stock/available for purchase, secondary distribution, or administration.

Most immunizers who responded to the survey (61 percent) had not depleted their inventory of influenza vaccine. Among those who had depleted their inventory and attempted to order additional doses, most were successful in obtaining additional doses. This information provided a helpful snapshot about vaccine available from different segments of the immunization community for the survey time frame.

Outreach and Communication

Over time, we have seen incremental improvements in overall flu vaccination coverage in the US, flu immunization coverage disparities among children have been eliminated, and substantial improvement has been made in vaccination coverage among pregnant women. Many factors contribute to public interest in flu vaccination, including some that we can not control, such as when disease activity begins, the severity of illness, and who is most impacted. However, outreach, communication and education efforts are essential tools for increasing vaccination coverage rates by increasing awareness about influenza, the populations recommended for vaccination, and other prevention and treatment options.

CDC's influenza communication and education efforts occur on an ongoing basis throughout the year and span all influenza topic areas, including disease activity; vaccine recommendations, safety and effectiveness; antiviral use; and vaccination coverage, among others. Activities begin in the spring with formative communication research and then continue in the summer with communication planning. Many of our National, State and local partners look to CDC's influenza communication plan and research findings to frame their own communication activities. These partners are critical to CDC's communication outreach efforts so continuous, year-round communication with them is essential. CDC relies on established partners (health provider organizations, medical institutions, and State, regional and local health departments) who all make an enormous effort to support CDC's annual campaign to promote flu vaccination, with special emphasis on those at greatest risk for complications from the flu and to reduce disparities. CDC also collaborates with a strong, active base of diverse multi-sector partners at national and local levels, including collaborating with community leaders to promote flu vaccination in underserved communities.

- Each year, CDC participates in a seasonal flu vaccination press event with the National Foundation for Infectious Diseases. This event typically involves sharing the final vaccine coverage data from the previous season, and promoting flu vaccination for the current season. This year's press event generated more than 1,030 print, online, and broadcast placements resulting in over 694 million impressions with media coverage by the [Associated Press](#), [Reuters](#), [New York Times](#), [USA Today](#), [HealthDay](#), [MedPage Today](#), [CBSNews.com](#), [NBC Nightly News](#) and [ABC World News](#).
- Our strategic partnership with Medscape and WebMD allows us to share important and timely influenza-related information through video commentaries on Medscape to raise the knowledge and awareness of clinicians of varied specialties about the importance of vaccinating their patients.
- CDC recognizes National Influenza Vaccination Week (NIVW) each year to highlight the importance of continuing influenza vaccination throughout the flu season, specifically before and after the holiday season, and into January and beyond. This year we announced an early start to flu activity. This event along with two National Radio Media Tours garnered approximately 88 million estimated impressions. In addition to these news media activities, a digital media outreach campaign garnered an estimated 157 million impressions through websites, blogs, tweets, live twitter chats, and mobile messages.
- This year, CDC also worked to educate the public about the significant burden flu illness has placed on the elderly this season. A spotlight article was posted on the CDC website that explained the significant increase in hospitalizations among people 65 years of age and older reported this season compared with last season, and emphasized that people 65 years of age and older are at high risk for serious complications from the flu and should seek early treatment from a doctor. CDC also created an article for seniors 65 years of age and older designed for placement in magazines or other publications, which was made freely available for download from the CDC website's "free flu resources webpage."
- In addition to traditional communication channels, CDC employs new technologies to reach a variety of new audiences, including social media and other new media. CDC recently launched our new Influenza iPad Application (App). Since the launch, there have been 99,100 page views of content by users of the new App and 8,010 downloads. CDC projects there will be approximately 130,000+ total page view of content by users during January 2013.
- CDC's seasonal flu website continues to be a valuable resource for sharing information with the public, health care professionals and other partners as evidenced by the Web metrics. This

season, the number of hits to the seasonal flu website began increasing significantly in December 2012 with 3.7 million views that month (average 141,000/day). This is three times the number of page views when compared to December 2011, and the highest number of views in 3 years. Web activity for January 2013 was nearly triple the December count, with 10.3 million page views (332,000/day). Among all content areas across CDC's website, influenza pages accounted for 7 of the top 10 page views. For the month of January, 15 percent of all web traffic for CDC.gov involved seasonal flu content.

The bottom line is that nearly 4 in 10 Americans get vaccinated each year. This is lower than we would wish though it is higher than any other country.

Antiviral Medications to Treat Influenza

Another important tool we have to prevent influenza related deaths and complications are antiviral medications – specifically the neuraminidase inhibitors. The benefits of antiviral drugs for treatment of influenza have been documented for some time. During and since the 2009 H1N1 pandemic, several observational studies demonstrated a reduction in serious influenza-related complications, such as pneumonia, respiratory failure necessitating ICU admission, and death, and a reduction in the length of hospitalization and duration of virus detection, with early antiviral treatment of hospitalized patients compared to no treatment or delayed treatment. Many of these studies included hospitalized patients, patients with underlying medical conditions and pregnant women. In randomized clinical trial studies of previously healthy patients with uncomplicated influenza, early treatment (within 48 hours of illness onset) with neuraminidase inhibitor antiviral drugs (oseltamivir and zanamivir) reduced illness by 1-2 days and lessened illness severity.

CDC is aware that questions have been raised about the clinical benefits of oseltamivir in reducing influenza-related complications. Specifically, a Cochrane Collaboration review of randomized control trials (RCTs) published last year generated some concern about the drugs. However, we believe a review of *all* available evidence demonstrates that early treatment with oseltamivir reduces influenza related severe outcomes, and CDC's guidance on the use of antiviral medications remains unchanged.

The ACIP and CDC consider all of the published evidence available from both RCT's and observational studies, including safety data, when issuing recommendations on antiviral treatment of influenza. ACIP and CDC guidance emphasize early antiviral treatment as soon as possible for patients who are hospitalized, severely ill and for those who are at greatest risk for complications from influenza. In our education and outreach efforts to clinicians, we emphasize both vaccination and antiviral treatment.

Preparing for the Next Influenza Pandemic

As I noted earlier, influenza viruses are constantly evolving and changing. Seasonal influenza viruses, the viruses that cause influenza in people every year, change from year to year and there is always some pre-existing background protection in the population. When a new influenza virus emerges, one that people have not previously been exposed to, and the virus has the ability to be transmitted from person to person, then we have the possibility of an influenza pandemic—widespread transmission of a new influenza virus against the background of very little if any pre-existing protection. The systems and the work that I have described today for seasonal influenza are exactly the systems and work we need to respond to an influenza pandemic. We need to detect the new virus, assess its ability to be transmitted

from person to person, develop and administer a vaccine, promote treatment with antiviral drugs, and communicate with the public and with the medical community. The more we can improve our seasonal influenza response, the more effective our response will be to a pandemic.

Conclusion

As we have been reminded this year, influenza is a serious disease and can result in hospitalization and death. The influenza virus is constantly evolving. At CDC we remain committed to keeping pace with influenza, improving our understanding of the disease and tools to prevent and treat it.

We continue to improve our surveillance of influenza, and have worked alongside our partners across the United States and the world to monitor those influenza strains currently circulating and detect those that emerge faster than ever. In close collaboration with our partners at FDA, NIH and other HHS components, we contribute to the evidence base to support the development and production of better influenza vaccines that can be produced more quickly.

As we have worked to improve surveillance and vaccines, we remain committed to sharing information with the general public and health care providers to prevent illness and death due to influenza through increasing vaccination coverage for all Americans and encouraging prompt treatment for those at high risk who do become sick with influenza. Thank you for your time today. I look forward to answering your questions.

Mr. MURPHY. Thank you, Dr. Frieden.
 Dr. Goodman, you are recognized for 5 minutes.

TESTIMONY OF JESSE GOODMAN

Dr. GOODMAN. Thank you. Mr. Chairman and members of the subcommittee, I am Jesse Goodman, Chief Scientist at the FDA and also a practicing infectious disease physician. I appreciate the opportunity to be here today and talk about FDA's role in protecting the public from influenza.

You know, flu seasons are quite unpredictable, and this year's season is a very telling reminder of how seriously we have to take flu, and as Dr. Burgess pointed out, I too have seen or heard of instances where even very healthy young people can be struck down by this disease. Some people tend to think what they have is a cold or something but most things that are colds are not influenza and most influenza can be quite severe and kill even healthy young people.

Our basic message is while this is a major public health problem we need to pay attention to, we have also made tremendous progress. To meet the threat of flu and other infectious diseases, we work very closely with our partners throughout the government in what we call the Public Health and Emergency Medical Countermeasures Enterprise, which includes numerous HHS partners as well as DOD, the VA, the USDA, etc. and the DHHS Assistant Secretary for Preparedness and Response.

This year, in response to this flu outbreak, we have expeditiously approved and released all available vaccines from six different manufacturers, and as Dr. Frieden said, and as reflected in the GAO report, this 140 million doses is a dramatic improvement from where we were a few years ago. We also helped divert shortages of antiviral medicines such as Tamiflu. We authorized the rapid release of 2 million doses in manufacturers' stockpile. We have also worked with the manufacturers and CDC so that pharmacists could use capsules to make liquid Tamiflu needed to treat small children, and that has been very helpful.

Unfortunately, every time we have a bad flu season, there is a bunch of unscrupulous people who come out of the woodwork with fraudulent flu products and try to take advantage of the public. So we have heightened our FDA surveillance of these various scams including looking at Web sites. We have taken action where needed and we have actually put information out to the public about fraudulent flu products that includes red flags they should look for in assessing these kinds of claims.

Now, with respect to vaccines, FDA doesn't make vaccines, but with influenza vaccine, we have a very unique and intimate working relationship with numerous partners to get the job done every year. Vaccine preparation is a very intensive, year-round, coordinated response involving working closely with manufacturers on almost a daily basis as well as with our global public health partners, WHO, CDC and others. It has numerous steps. I won't go through here based on time, and manufacturers exhaustively test their vaccines and submit results.

Now, why we are testifying here today, in part, is because of this virus. This is a unique virus. It is constantly changing. It is a

crafty and unpredictable virus. The surface proteins on the virus are changing all the time and that helps it evade our immune systems and it also helps it evade our vaccines, which is part of the challenge there. Ten years ago, we had only three U.S.-licensed influenza vaccine manufacturers. We initiated significant efforts including a new accelerated approval pathway to increase the diversity and amount of vaccine supply as well as to upgrade manufacturer quality and hopefully do all we can to prevent failures in manufacturing. As a result, we now have seven vaccine manufacturers and an approximate doubling of supply.

In addition, I would say as a result of substantial ASPR, BARDA and industry investment and very intense interactions with FDA, as you have heard, we have two recent innovative flu vaccine approvals. The first is Flucelvax, made by Novartis, the first U.S.-licensed cell-based flu vaccine. The advantages of the cell-based vaccine include elimination of the need for a large number of fertile eggs, which can be a problem if there were an avian flu outbreak, better growth of strains that sometimes grow poorly in eggs, and faster startup and scale of manufacturing. Also good news is that Novartis is planning to manufacture this in their new facility at Holly Springs, North Carolina, that was built with a lot of ASPR and BARDA support as well and will substantially increase U.S. manufacturing capacity.

The other new vaccine is Flublok, manufactured by Protein Sciences, again developed with government support, and it is the first influenza vaccine using recombinant DNA technology. This is produced using an insect virus grown in insect cells to produce the flu virus protein. It can be manufactured just based on the genetic sequence of the virus. We don't need a living virus at all in order to produce the vaccine, which can therefore be obtained within days instead of weeks. In a time-limited situation like a pandemic, this could be very advantageous.

We have also worked with BARDA to retrofit existing manufacturing facilities to increase their surge capacity. Recently FDA is working with BARDA in a collaborative way to provide technical assistance in three very exciting recently funded centers called Centers for Innovation in Advanced Development and Manufacturing located in Texas, North Carolina, and Maryland.

You probably have heard about the need for more effective flu vaccines, and this is also a high priority for FDA. There are a number of promising approaches under active research and development for this technology. They are not here today but we are hoping to get there. These include efforts to induce a stronger, more effective, longer lasting immune response that could protect against viruses that change over time. As another strategy, there are efforts going on directing vaccines against recently identified parts of the virus's genes that are conserved among multiple strains.

Another thing we are doing is trying to improve diagnostics. Accurate diagnostics are incredibly important. They can avoid unneeded use of antivirals and antibiotics, and as well, we are trying to facilitate development and use of the antiviral drugs.

In conclusion, we have come a long way in enhancing our ability to prepare for and respond to influenza. We are fully engaged in an ongoing, intensive effort to enhance our Nation's preparedness.

We are much better prepared. There have been several landmark recent approvals and new science is developing that promises a bright future.

I did want to mention that the response to influenza is every single year a remarkable public-private partnership. We are all working together, and I am optimistic that the gains that have been made are on track to continue. Thank you very much.

[The prepared statement of Dr. Goodman follows:]



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

**STATEMENT
OF
JESSE L. GOODMAN, M.D., MPH
CHIEF SCIENTIST
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES**

“Influenza: Perspective on Current Season and Update on Preparedness”

**BEFORE THE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
COMMITTEE ON ENERGY AND COMMERCE
U.S. HOUSE OF REPRESENTATIVES**

February 13, 2013

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INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Dr. Jesse Goodman, Chief Scientist at the Food and Drug Administration (FDA or the Agency). I am also a practicing Infectious Diseases physician. Thank you for the opportunity to be here today with my colleague from the Centers for Disease Control and Prevention (CDC) to discuss FDA's role, working with partners throughout government and the private sector, in protecting the public from influenza—one of the most serious infectious disease threats to our nation.

Flu seasons are unpredictable and this year's H3N2 seasonal flu epidemic is a telling reminder of the continuing challenge of influenza and the need for individuals worldwide to take seasonal influenza very seriously. Seasonal influenza causes substantial illness and death, not only posing high risk to the elderly, but also to pregnant women, infants, and children. While influenza remains a major challenge in ways I will touch on later, our nation has made tremendous progress in preparedness for seasonal and pandemic flu, particularly since the 2009 H1N1 pandemic.

FDA's overall responsibility, with respect to influenza, is helping to ensure that medical countermeasures (MCM) used to diagnose, prevent, and treat influenza—including drugs, vaccines, and diagnostic tests—are safe, effective, and secure. FDA also works with manufacturers and other stakeholders in their efforts to enhance the development and availability of new products to fulfill unmet public health needs, including the application of regulatory science to improve the diagnosis, prevention, and treatment of influenza. In meeting the challenge of flu, and in preparing for and responding to other infectious disease threats, including

the threat of bioterrorism, FDA works closely with its partners within the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE),¹ as well as with manufacturers and global regulatory and public health partners.

In responding to this year's influenza epidemic, FDA has been working closely with CDC, industry, and other stakeholders to make as much vaccine as possible available to the public in a timely way and to enhance the supplies of needed diagnostics and antivirals to help diagnose and treat those who do get influenza. FDA has approved and lot-released all available influenza vaccine from six manufacturers, who collectively produced more than 140 million doses for the United States—far more than was available only a few years ago. This vaccine is well-matched to the circulating virus causing most influenza disease this year.

Although some regions of the country have experienced spot shortages of flu vaccine, this is due to increased public attention and high demand brought on by a flu season that arrived early and forcefully. In addition to doing all that is possible to facilitate access to vaccine, FDA is working closely with CDC and other agencies and offices within our mutual parent agency, the Department of Health and Human Services (HHS), and manufacturers to monitor and help address potential shortages. For example, faced with a shortage of the antiviral, liquid Tamiflu (oseltamivir), for young children, FDA worked with CDC and the manufacturer to provide information to pharmacists to safely prepare liquid Tamiflu from Tamiflu capsules. Further, FDA has exercised regulatory flexibility with respect to the rapid release of 2 million Tamiflu

¹This includes FDA, the National Institutes of Health (NIH), CDC, the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR), the Department of Defense (DoD), the Department of Homeland Security, the Department of Veterans Affairs, and the Department of Agriculture.

capsules that had been held in reserve. FDA also has generated data to show that properly stockpiled Tamiflu supplies can remain usable for up to 10 years beyond their date of manufacture and has made public health authorities aware that FDA will exercise enforcement discretion with respect to use of these stockpiled reserves, if they are needed.

As the current influenza outbreak spread, FDA anticipated a proliferation in the promotion of fraudulent products for prevention and treatment. FDA significantly increased its surveillance of online promotions for unapproved flu products, which come in a variety of forms, including supplements, conventional foods, and unapproved drugs and devices. Of particular concern are products promoted as alternatives to the flu vaccine and unapproved antiviral drugs sold by illegitimate online pharmacies. FDA considers the promotion of unapproved products to prevent or treat the flu to be a potentially significant threat to public health, and responsible firms may be subject to regulatory and enforcement actions. FDA also has issued a “Beware of Fraudulent Flu Products” article to alert consumers about fraudulent flu products and “Red Flag” promotional claims to watch out for.

FDA’s Role in the Development of Vaccines to Prevent Influenza

FDA does not make vaccines; however, each and every year we play a unique and critical role in facilitating influenza vaccine production and availability. Preparing for each year’s influenza season is an intensive, time-critical, and highly orchestrated and collaborative effort involving FDA, CDC, the World Health Organization (WHO), vaccine manufacturers, and the public health community. It is a year-round process that requires worldwide influenza surveillance, selection of virus strains, preparation of antigens and reagents for vaccine manufacturing, approval of each year’s vaccines as a strain change supplement to their licenses, and the testing,

lot release, and distribution of over 100 million doses of vaccine, followed by continual safety monitoring.

Influenza is a very challenging virus in that its surface proteins change constantly to evade both our immune systems and vaccines. As a result of these changes, in most years, at least one of the strains in the vaccine must be changed to keep up with changes in the circulating virus. Over 100 million doses of vaccine must be manufactured each year for the United States in a short period of time; almost every year it is a somewhat different vaccine and can present unique manufacturing challenges. Since the virus is so unpredictable, and vaccine production is complex, FDA must be continuously alert and adaptable.

The U.S.-licensed seasonal influenza vaccines currently in use are made based on representative strains of three (trivalent) influenza viruses—two influenza A strains (H1N1 and H3N2) and one B strain, or more recently, the quadrivalent vaccine that includes an additional B strain and will be available beginning next flu season. These are selected to protect against the strains that, based on worldwide surveillance, are likely to cause the most human infection during the upcoming season. FDA selects the appropriate strains with input from our Vaccines and Related Biological Products Advisory Committee and relies on a global disease surveillance effort led by WHO. CDC is a major participant in this surveillance effort.

Currently available influenza vaccines contain either purified hemagglutinin (HA), a surface protein of the influenza virus against which the human body directs much of its immune response, or a live version of a highly weakened, modified influenza virus. These vaccines, neither of which can cause flu, are referred to as inactivated or live-attenuated influenza

vaccines, respectively. Influenza vaccines have a proven safety record over many years of use in hundreds of millions of individuals annually; serious adverse events are very rare.

The effectiveness of influenza vaccines is lower than that for other vaccines and lower than we would prefer from a public health perspective. Their effectiveness, however, is still significant and, when well-matched to circulating strains, they are effective at protecting the majority of those vaccinated. CDC's preliminary estimate for this year is that vaccinated individuals had 60 percent fewer cases of confirmed influenza than did unvaccinated individuals. Influenza vaccine is most effective in healthy young people and typically less effective in the elderly, particularly those who have chronic diseases and whose immune systems may not typically respond well to either influenza or influenza vaccines. However, given their high risk of complications from influenza disease, vaccination is still highly recommended for the elderly. Live-attenuated influenza vaccine is indicated for healthy individuals, ages 2 to 49.

An important point to emphasize is that symptoms suggesting influenza can be caused by multiple other viruses as well as bacteria, and the majority of respiratory illnesses, particularly mild ones, are not due to influenza. Thus, it is not surprising for individuals to receive the flu vaccine and still get a seemingly flu-like respiratory illness. While influenza vaccines cannot prevent these other infections and the current vaccines cannot completely protect everyone from influenza, they are still our safest and most effective measure to prevent this life-threatening disease. Thus, CDC recommends that nearly all people over 6 months of age receive flu vaccine.

Vaccine Production

Each year, FDA begins working with manufacturers at the earliest stages of vaccine development and continues to interact with them throughout production. After strain selection, which

typically occurs each February, the reference influenza viruses are sent from a WHO Collaborating Center to the licensed vaccine manufacturers to generate “seed virus” banks used to produce the vaccines. FDA develops and calibrates “reference reagents,” which are provided to vaccine manufacturers and to our regulatory counterparts throughout the world. These reagents are essential to test the inactivated vaccines for potency and to formulate standard dosages. FDA evaluates each strain of inactivated virus and the manufacturers then formulate the bulk vaccines. Manufacturers submit samples to FDA for testing along with results of their own testing. FDA reviews this information and conducts its own testing prior to releasing any formulated bulk vaccine lots. Manufacturers then fill and finish the vaccines into vials and syringes, or, for live-attenuated vaccine, into nasal sprayers. Manufacturers exhaustively test their influenza vaccines, including for potency, purity, and sterility, prior to distribution. The process of lot release and vaccine distribution continues through the fall and early winter. This influenza season, FDA released all lots of influenza vaccine by early December. Egg-based vaccines typically require about six months for complete vaccine production each season.

Efforts to Increase Influenza Vaccine Manufacturing Capacity and Supply

Ten years ago, there were only three U.S.-licensed influenza vaccine manufacturers. In 2004, significant manufacturing difficulties with one manufacturer resulted in limited supplies. To better insure against future problems, FDA initiated significant efforts to increase both the diversity and amount of the vaccine supply and to upgrade manufacturing oversight and quality industry-wide.

From 2004-2007, working with the Office of the Assistant Secretary for Preparedness and Response (ASPR), Biomedical Advanced Research and Development Authority (BARDA), HHS

and major manufacturers of influenza vaccine throughout the world, we achieved a doubling of the number of U.S.-licensed manufacturers (from three to six—on January 16, 2013, we approved a seventh) and an approximate doubling of vaccine manufacturing capacity and supply. FDA accomplished this by stimulating interest in production for the U.S. market and by utilizing an accelerated approval pathway to speed the evaluation and licensure of new influenza vaccines.

Recent Developments in Influenza Vaccine Production

As a result of substantial ASPR/BARDA investment and intense interactions with FDA, two novel influenza vaccines made with alternative manufacturing technologies were approved recently. These vaccines will supplement the supply of seasonal vaccines, and the new technologies offer the potential for faster start up of vaccine manufacturing for future pandemic threats.

Flucelvax, approved in November 2012, is the first U.S.-licensed flu vaccine manufactured using cell-culture technology instead of fertilized chicken eggs. Potential advantages of cell-culture technology include: (1) elimination, through use of well-characterized and readily available cells, of the need for large numbers of fertile eggs (which could be threatened, for example, by an avian flu outbreak); (2) the potential for manufacturing influenza vaccine using strains of virus that do not grow well in eggs; and (3) the potential for faster start-up and scale-up of manufacturing in the event of a pandemic. Currently, the cell-based Flucelvax vaccine is manufactured by Novartis in Germany, but they plan to eventually move production to the cell-based facility in Holly Springs, North Carolina, built with ASPR/BARDA support and extensive FDA technical assistance. This facility significantly increases both overall and U.S.-based manufacturing and capacity.

Flublok, manufactured by Protein Sciences Corporation (PSC) and also developed with support from ASPR/BARDA and NIH, was approved in January 2013. It is the first U.S.-licensed flu vaccine manufactured using recombinant DNA technology. Flublok also does not require eggs, nor is it necessary for PSC to have the influenza virus available to begin production of Flublok. Flublok's novel manufacturing technology uses an insect virus grown in insect cells to produce the HA protein subsequently used to produce the influenza vaccine. It can be manufactured simply based on the HA genetic sequence of any desired flu virus, something that can be obtained and verified within days. This affords a potential significant advantage over previously licensed technologies in an emergency because the production of reference virus strains, which can be a significant time-limiting factor in responding to a pandemic or other outbreak, is not needed. Recombinant and molecular DNA expression technologies, including those being supported by ASPR/BARDA, have started to allow approaches that do not depend on virus growth to be used for production of influenza vaccines, and these technologies could serve as platforms for production of other vaccines as well.

FDA also has worked with BARDA to retrofit manufacturing facilities to increase existing domestic egg-based flu vaccine production surge capacity. These successes in developing increased domestic production capacity and novel non-egg-based production techniques are particularly important in enhancing readiness to rapidly produce large amounts of vaccine in response to an emerging pandemic. To this end, FDA is collaborating with ASPR/BARDA to provide technical assistance to BARDA-funded Centers for Innovation in Advanced Development and Manufacturing (ADM). These Centers were established specifically to increase U.S. domestic vaccine surge production capacity in response to a pandemic or other

emerging threat and offer a new model for public-private partnerships, bringing together small biotech companies, academic institutions, and large experienced pharmaceutical companies. Production sites include those in Texas, North Carolina, and Maryland, and will use modern technologies for accelerating production, improving quality, and expanding domestic vaccine manufacturing capabilities.

FDA is working closely with ASPR/BARDA and the ADM sites to provide technical advice to facilitate high-quality development and manufacturing and, ultimately, regulatory approval. Similarly, FDA has provided expertise to the Department of Defense's ADM programs and to the Defense Advanced Research Projects Agency (DARPA) in their efforts to rapidly manufacture plant-based influenza vaccines.

In addition to helping us better prepare for influenza pandemics, these new production approaches and facilities will increase our nation's agility and capacity to respond to other, unanticipated infectious disease threats, natural or man-made.

Process Improvements Through Regulatory Science

In addition to enhancing vaccine production and U.S.-based capacity, with the support of Congress, and as highlighted in Secretary Sebelius' 2010 Medical Countermeasure Review, FDA has significantly expanded its infrastructure to support increased capacity for rapid testing and lot release of influenza vaccines and for targeted regulatory science. For example, the Agency developed a technique for rapid sterility testing that provides results almost three times faster than previous assays. To facilitate adoption of these new rapid sterility methods, FDA amended its regulation regarding sterility testing to provide more flexibility while ensuring continued

safety. Further, FDA is collaborating with HHS, CDC, and NIH to develop new potency tests and more rapid ways to make potency reagents, which would help make both seasonal and pandemic influenza vaccines available more quickly. Taken together, all of these approaches are helping to safely reduce the time needed to produce a vaccine and make it available.

Improved Influenza Vaccines

While all of these efforts have better prepared us for both seasonal influenza and future pandemics, we also need more effective flu vaccines. This is a high priority across the PHEMCE. Although HHS funding and programmatic activities in this area are largely directed by NIH and ASPR/BARDA, given the importance of such efforts, I will briefly mention them here. An ideal influenza vaccine would be effective in preventing flu after a single dose, even in individuals with weakened immune systems who are most at risk, such as the elderly and those with chronic diseases. It would provide strong immunity that lasts beyond a single season and protects not just against the strains of flu the vaccine is based on, but against the altered strains of flu that continuously evolve. Ideally, it could also afford at least some protection against markedly different flu viruses that arise and have major pandemic potential. When needed, large amounts of such a vaccine could be produced rapidly.

While we currently do not have vaccine candidates with all of these characteristics, there are a number of promising approaches under active research and development supported by the U.S. Government and/or by industry. These include use of novel adjuvants—substances added to a vaccine that can boost the immune response of the individual. Some adjuvanted candidate vaccines appear to stimulate a much stronger immune response, including against H5 avian influenza for which existing flu vaccines only stimulate a weak response. Novel adjuvants also appear potentially able to stimulate a broader immune response, e.g., a response that works better

than current vaccines against viruses that have changed from the strain included in the vaccine. Many studies are still under way regarding adjuvanted vaccines and their potential for influenza, including studies at FDA's Center for Biologics Evaluation and Research concerning both adjuvant effects on the immune response and on safety. Novel adjuvants have been stockpiled with ASPR/BARDA support, in case they are needed for a severe pandemic.

Other novel approaches which may improve the immune response to flu vaccines include the use of virus proteins packaged in virus-like particles, a type of approach already used in licensed vaccines to prevent cervical cancer. Also, approaches using DNA-based vaccines, or use of DNA and protein vaccines in sequence, may enhance the immune response and provide novel approaches to rapid vaccine production. In addition to these novel approaches to enhance immunity through new vaccine technologies, NIH, ASPR/BARDA, and industry are supporting efforts to make vaccines using parts of the virus that do not change as much from strain to strain, including well-conserved parts of the HA gene and a number of other genes. These approaches are often grouped together as "universal flu vaccines" for the potential they may offer to protect against multiple flu strains. FDA is working with innovators to facilitate development of such products.

Vaccine Safety Monitoring

Robust safety monitoring is critical, both to ensure the continued safety of vaccines and to maintain public confidence. FDA monitors influenza vaccine post-licensure and reviews, interprets, and analyzes adverse event reports collected through the Vaccine Adverse Event Reporting System (VAERS). In collaboration with the Centers for Medicare and Medicaid Services (CMS), FDA conducts near real-time monitoring for Guillain-Barre Syndrome (GBS), a rare adverse event of high interest because of its unexpected association with swine flu vaccine

in 1976. In addition, FDA collaborates with CDC to perform studies and rapid-cycle analysis as needed through CDC's Vaccine Safety Datalink (VSD), an active surveillance system with nine health maintenance organizations. During the 2009 H1N1 pandemic, FDA, in collaboration with CDC, DoD, Department of Veterans Affairs, CMS, and regulatory counterparts around the world, implemented aggressive, near real-time safety monitoring, including for GBS, with rapid-cycle analysis of numerous data sources. This allowed active detection and follow-up of any potential safety signals and was instrumental in addressing potential concerns as they arose. To further enhance safety surveillance, FDA is developing the Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program, the largest electronic real-time active surveillance system for vaccine safety in the United States.

Development and Review of Tests to Diagnose Influenza

Given that so many different infections can present similarly to influenza, accurate, sensitive, and convenient diagnostic tests for influenza are important. Accurate diagnosis is critical to treating influenza effectively. Accurate diagnosis also limits unneeded use of antivirals and antibiotics, conserves needed drugs, and reduces the risk of resistance. Enhancing the availability, performance and use of influenza diagnostics is the subject of considerable interest across the PHEMCE. The lessons learned from the 2009 pandemic were transformative. FDA made 18 tests available under Emergency Use Authorizations, strengthening interactions with manufacturers and collaborations with CDC and other federal partners. In addition, these stakeholders continue to work together to fill critical gaps, such as the need for appropriate specimens for manufacturers to validate their diagnostic tests.

FDA also has been working with CDC, HHS, and manufacturers to help improve the sensitivity of rapid influenza tests, including the ability to better adapt to the changing influenza strains that

circulate each season. This collaboration has led to comparison testing studies of devices and CDC guidance to inform physicians how to best use and interpret these tests.

FDA continues to work with manufacturers to facilitate research and development and to review and approve new influenza diagnostic tests. This includes work to help stimulate the development of highly multiplexed tests to simultaneously detect multiple types of organisms, including influenza virus, in order to accurately diagnose the specific cause of a patient's disease. Congress' support of the MCM initiative has been important to these efforts.

In November 2012, FDA published a draft guidance document for the validation of highly multiplexed tests and is now using newly developed scientific/regulatory processes for reviewing submissions for highly multiplexed tests. Since the 2009 pandemic emergency was terminated, FDA has cleared a total of 16 new influenza tests, four of which were rapid tests.

Development of Antivirals to Treat Influenza

Antiviral drugs are used to treat people with flu to reduce the severity and duration of disease. There are four FDA-approved antivirals, including two currently being used to treat (or, in certain circumstances, to prevent) seasonal influenza: Tamiflu and Relenza (zanamivir). FDA works closely with its HHS partners, including NIH and ASPR/BARDA and the manufacturers, to monitor and review information relevant to the effectiveness, safety, and availability of antivirals in order to enhance their use. In December 2012, FDA approved oseltamivir dosing for use in children between 2 weeks and 1 year of age, making it the first influenza antiviral approved for children younger than 1 year old. In addition, FDA has worked to assess the stability of these drugs, helping to improve the information base for their inclusion in the U.S. Strategic National Stockpile, which serves as an emergency back up for commercial supplies.

FDA is conducting research to evaluate how varying shipping and storage conditions affect antiviral drugs, which will inform future stockpiling decisions.

FDA also recognizes the need for new and improved influenza drugs, including intravenous drugs, to address, for example, drug resistance and treatment needs for severe illnesses. The development of these products is challenging and complex. To help product developers, FDA released a guidance document entitled “Influenza: Developing Drugs for Treatment and/or Prophylaxis” in 2011. In addition, the Agency works closely with innovators to provide feedback on proposed development plans and clinical trial designs.

When individual patients are seriously ill and the treating clinicians believe there is a need to use antiviral drugs that are still under development (e.g., intravenous formulations), FDA works with treating clinicians and manufacturers to facilitate access to drugs under expanded-access processes, if there is an unmet need that requires use of the investigational drug outside of the existing clinical trials. It is important to note that providing expanded access on an individual basis generally does not provide reliable information about treatment effects. Controlled clinical trials are important for overall assessment of the risks and benefits of new antivirals. They do not always show the benefits that had been hoped for, based on preliminary information. Even trials with less-than-hoped-for outcomes can be a source of learning to improve the approach to future drug development.

CONCLUSION

FDA plays a key role, working closely with our government partners and with industry, in facilitating the development, evaluation, and availability of safe and effective measures to diagnosis, treat, and prevent influenza. We have come a long way in enhancing our ability to

prepare for and respond to both seasonal and pandemic influenza, and we are fully engaged in an ongoing and intensive effort to further enhance our nation's preparedness and response. The response to influenza is, year after year, a public-private partnership.

I want to note how important the capacity and engagement of our public health and health care systems are for detecting and responding to major events for influenza and other threats. For influenza, a strong surveillance system can help improve the odds that the vaccine produced each year will be effective, and, even more important, help detect earlier the emergence of a pandemic. A coordinated response, with public health, health care organizations, industry, and government working together, much like we saw in the response to the 2009 pandemic, is what we need to protect our nation against these threats.

FDA's MCM Initiative, supported by Congress, has helped us play an active engaged role in public health preparedness and response, supporting highly interactive relationships. We are much better prepared, have achieved several recent landmark developments and product approvals, and developed new science that promises a bright future. We are all working together and I am optimistic that the gains that have been made are on track to continue.

Thank you, again, for the opportunity to testify on this issue. I welcome your input and questions.

Mr. MURPHY. Thank you, Dr. Goodman.
Dr. Crosse, you are recognized for 5 minutes.

TESTIMONY OF MARCIA CROSSE

Ms. CROSSE. Thank you, Chairman Murphy, Ranking Member DeGette and members of the subcommittee. I am pleased to be here today as you examine issues related to the current influenza season and influenza preparedness.

As we have already heard, this season there has been early and intense influenza activity throughout much of the country with some spot shortages of vaccine. My remarks today focus on lessons learned from federal responses to prior influenza outbreaks and federal investments to strengthen the U.S. vaccine supply. My testimony is based on multiple GAO reports on seasonal and pandemic influenza. Our prior work has identified a number of lessons from the response to seasonal vaccine shortages and the 2009 H1N1 pandemic and actions the government has taken to improve the vaccine supply.

The primary lessons we observed can be grouped into four broad interrelated categories: the value of planning, the importance of effective communication, the difficulties in predicting the predominant influenza virus strains that will be circulating in a given season, and the challenge of matching available vaccine supply with public demand.

First, planning is critical to an effective response. For example, planning activities conducted prior to the H1N1 pandemic such as exercises and interagency meetings built relationships among federal, State and local governments and positioned them to respond effectively. This type of planning is especially important in years when there are vaccine shortages or when there are specific groups for which vaccine must be prioritized.

Second, clear and consistent communication is key, especially regarding the availability of vaccine. The failure to effectively manage public expectations of vaccine availability can undermine government credibility and contribute to individuals' failure to seek vaccination. This has been a problem in years when vaccine is in short supply or is delivered later than anticipated, but it can even be a problem in years with no shortage, such as this year, if individuals are uncertain of when or where to obtain vaccine.

Third, predicting the influenza virus strains that will predominate in a given season and their likely severity is difficult. Because the selection of the three viral strains normally included in the vaccine is typically made in February, in some years the vaccine may not be well matched to all the strains that are circulating during the following winter. A positive development is that FDA recently approved two new vaccines that each protect against a total of four influenza strains, one more strain than traditional seasonal vaccines. These new vaccines are expected to be available for the next influenza season.

And fourth, matching influenza vaccine supply to demand is challenging. Because of the lengthy production cycle, manufacturers make production decisions months in advance of a seasonal outbreak, and vaccine supply orders are generally placed before providers know what the severity of the outbreak will be. Manufactur-

ers may be reluctant to produce and providers may be reluctant to order vaccine that exceeds their projected demand because if the product is not used by the end of the season, it must be destroyed.

Over the last decade, HHS has taken steps to strengthen the influenza vaccine supply by making investments in the development of alternative vaccine production technologies and by enhancing domestic production capacity. Since 2005, HHS has awarded over \$1 billion in contracts to manufacturers to develop new influenza vaccines that rely on cell-based or recombinant technologies, and two of these alternative vaccines are expected to be available for the next influenza season.

In summary, over the last decade progress has been made in the federal government's preparation for and response to both seasonal and pandemic influenza events. Planning activities have helped with response efforts, communication with the public regarding where and when to get vaccine has been clearer and more effective, and manufacturers have been encouraged to enhance domestic production capacity and develop alternative production technologies. Yet the fact remains that when facing a typical influenza season, manufacturers must make decisions about how much vaccine to produce, providers must determine how much vaccine to order, and individuals who may be influenced by a particular season's perceived severity and media reports must make their own decisions about whether, when and where to seek vaccination. These factors along with challenges inherent in the vaccine production process and influenza seasons that are unpredictable in terms of duration and severity can still present barriers to successfully making vaccine available when and where it is needed.

Mr. Chairman, this concludes my prepared remarks. I would be happy to answer any questions that you or other member of the subcommittee may have.

[The prepared statement of Ms. Crosse follows:]

United States Government Accountability Office

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Testimony

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INFLUENZA

Progress Made in
Responding to Seasonal and
Pandemic Outbreaks

Statement of Marcia Crosse
Director, Health Care



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Highlights

Highlights of GAO-13-374T, a testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives

Why GAO Did This Study

Influenza—in both its seasonal and pandemic forms—is an ongoing public health concern. In the United States, seasonal influenza has been associated with thousands of deaths each year, according to CDC. In a pandemic, such as the 2009 H1N1 influenza pandemic, the disease causes a global disease outbreak with the potential for many more deaths. HHS has responsibility for coordinating the nation's response to public health emergencies, including an influenza pandemic. Within HHS, CDC makes recommendations on vaccination, tracks the disease, and disseminates public health messages on influenza. This testimony discusses (1) lessons learned from federal responses to prior influenza outbreaks and (2) federal investments to strengthen the U.S. vaccine supply and production capacity.

This testimony is based on prior GAO work on issues related to influenza vaccine supply and distribution; federal investments in domestic vaccine production capacity and production technologies; and the federal response to the 2009 H1N1 pandemic. This prior work includes analyses of information and interviews with officials within HHS, CDC, and FDA, as well as officials from vaccine manufacturers, medical supply distributors, state and local governments, provider groups, and other stakeholders. GAO also obtained updated information from HHS on the severity of the past three seasons, the numbers of vaccine doses distributed, and the status of advanced vaccine technology projects funded by HHS. HHS reviewed updated information and provided technical comments, which are incorporated as appropriate.

View GAO-13-374T. For more information, contact Marcia Crosse at (202) 512-7114 or crosse.m@gao.gov.

February 2013

INFLUENZA

Progress Made in Responding to Seasonal and Pandemic Outbreaks

What GAO Found

GAO's prior work has identified a number of lessons from federal responses to seasonal influenza vaccine shortages and the 2009 H1N1 pandemic that carry implications for future influenza seasons or another influenza pandemic. These lessons include the value of planning that involves the Department of Health and Human Services (HHS); the importance of effective communication among all levels of government and with the public; and the difficulty of matching vaccine supply with the public's demand for it. First, planning is critical to an effective response, and it particularly helped in responding to the H1N1 pandemic. Planning activities, such as exercises and interagency meetings, built relationships that positioned the government to respond effectively. Second, clear and consistent communication, especially regarding the availability of vaccine, is key. The failure to effectively manage public expectations of vaccine availability can undermine government credibility and contribute to individuals' failure to seek or receive an influenza vaccination. Recognizing the importance of sharing updated information, HHS's influenza website includes a vaccine finder for individuals, and the Centers for Disease Control and Prevention's (CDC) website helps providers find vaccine available for purchase. Third, predicting all of the influenza virus strains that will be circulating in a given season and their likely severity is difficult. Finally, matching influenza vaccine supply to demand is challenging, as the supply of and demand for vaccine can vary throughout seasons and across multiple seasons. HHS has taken a number of steps to address these lessons learned; however, the department continues to face challenges, particularly in communicating messages in changing circumstances and in facilitating the matching of available vaccine supply with public demand.

HHS has taken steps to strengthen the U.S. influenza vaccine supply by making investments in the development of vaccine production technologies and by enhancing domestic production capacity. Influenza vaccine has generally been produced in a complex egg-based process that poses limitations in timeliness and the susceptibility of the egg supply to certain influenza viruses. Prompted by these disadvantages, HHS has made investments in alternative vaccine production technologies, including cell-based and recombinant technologies. Since fiscal year 2005, HHS has awarded over \$1 billion in contracts to manufacturers to develop cell-based technology. One of these manufacturers recently received approval from HHS's Food and Drug Administration (FDA) for its cell-based seasonal influenza vaccine, which it intends to produce for the 2013–2014 influenza season. In addition, in fiscal year 2009, HHS entered into a contract worth approximately \$81 million with one manufacturer for the continued development of recombinant technology; that manufacturer's seasonal influenza vaccine made using this technology is expected to be available for the 2013–2014 influenza season. HHS has complemented its investments in vaccine production technologies with its investments in domestic manufacturers' production capacity. Since fiscal year 2005, these investments have contributed to the doubling of the number of domestic influenza vaccine manufacturers and a general increase in the number of influenza vaccine doses produced and distributed.



United States Government Accountability Office
Washington, DC 20548

Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee:

I am pleased to be here today as you reflect on the current influenza season and examine issues related to influenza preparedness. Influenza, in both its seasonal and pandemic forms, is an ongoing public health concern. In the northern hemisphere, seasonal influenza may begin as early as August and generally diminishes by April. It has been associated with 3,000 to nearly 50,000 deaths each year in the United States in recent decades, according to the Department of Health and Human Services's (HHS) Centers for Disease Control and Prevention (CDC).¹ In a pandemic, such as the recent 2009 H1N1 influenza pandemic, influenza causes a global disease outbreak with the potential for many more deaths than in a typical influenza season.²

My remarks today focus on (1) lessons learned from federal responses to prior influenza outbreaks and (2) federal investments to strengthen the U.S. vaccine supply and production capacity. My testimony is based on multiple GAO reports and testimonies in relation to seasonal and pandemic influenza.³ Specifically, this body of work includes issues related to influenza vaccine supply, distribution, and shortages; federal investments in the U.S. vaccine supply and alternative technologies for influenza vaccine production; and the federal response to the 2009 H1N1 pandemic. This prior work includes analyses of information and interviews with officials within HHS, such as those from CDC and the Food and Drug Administration (FDA); as well as officials from influenza vaccine manufacturers, medical supply distributors, state and local governments, provider groups, and national associations such as the Association of State and Territorial Health Officials. In preparation for this testimony, we obtained updated information from HHS, including on the numbers of

¹CDC, "Estimates of Deaths Associated with Seasonal Influenza—United States, 1976–2007," *Morbidity and Mortality Weekly Report*, vol. 59, no. 33 (2010): 1057–1062.

²Pandemics occurring in the past 100 years include the "Spanish flu" of 1918, which killed an estimated 675,000 people in the United States; the "Asian flu" of 1957, responsible for approximately 70,000 deaths in the United States; the "Hong Kong flu" of 1968, which caused an estimated 34,000 deaths in the United States; and the 2009 H1N1 pandemic, which caused from 8,870 to 18,300 deaths in the United States. Influenza pandemics can have successive "waves" of disease and last for up to 3 years.

³See a list of related GAO products at the end of this statement.

vaccine doses produced and distributed, the severity of the past three seasons, and the status of advanced technology projects funded by HHS. We conducted our work in accordance with generally accepted government auditing standards.⁴ Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings based on our audit objectives. We provided HHS with a copy of updated facts in this statement for its review. HHS provided technical comments, which we incorporated as appropriate.

Background

Influenza is characterized by cough, fever, headache, and other symptoms and is more severe than some viral respiratory infections, such as the common cold. Most people who contract seasonal influenza recover completely in 1 to 2 weeks, but some develop serious and potentially life-threatening medical complications, such as pneumonia. Groups at higher risk of developing serious influenza-related complications include those aged 65 years and older; those with chronic medical conditions; young children, particularly those under 2 years of age; and pregnant women. During an influenza pandemic, different groups may be affected. For example, some past influenza pandemics have affected healthy young adults who are not typically at high risk for severe influenza-related complications.

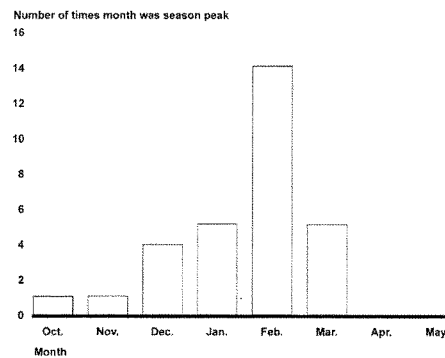
Annual vaccination is the main method for preventing seasonal influenza. Since 2010, CDC and its Advisory Committee on Immunization Practices have recommended annual influenza vaccinations for everyone aged 6 months or older.⁵ After vaccination, the body takes about 2 weeks to produce the antibodies that protect against infection. Vaccination in the fall, before the U.S. influenza season begins, is preferable; however, because influenza in the United States typically begins to increase in late December or early January and peaks in February most seasons,

⁴We conducted our work from November 2000 to June 2011, and February 2013. See the list of related products at the end of this statement for more information on our work.

⁵Some people should not get a flu vaccination without first consulting a physician, including people who have had a severe reaction to an influenza vaccination and people who have a severe allergy to chicken eggs. See <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6132a3.htm> for ACIP's recommendations for the 2012–2013 influenza season (accessed Feb. 7, 2013).

vaccination in December or later can still be beneficial. The influenza season peaked in February in nearly half (14) of the influenza seasons over the past three decades (see fig. 1).

Figure 1: Month of Peak Influenza Activity, 1982–1983 through 2011–2012 Seasons



Source: CDC.

Note: This figure shows peak influenza activity for the United States, by month, for the 1982–1983 through 2011–2012 seasons.

Within the federal government, HHS has primary responsibility for coordinating the nation's response to public health emergencies, such as an influenza pandemic. Additionally, as the principal department for protecting the nation's public health, HHS is the primary department funding the research and development of influenza vaccines. Within HHS, CDC makes recommendations on who should be vaccinated, tracks the spread of influenza and vaccination rates, and disseminates public health messages encouraging vaccination and other protective measures, such

as hand washing. FDA is responsible for selecting the influenza strains to include in the annual influenza vaccines and for licensing vaccines.⁶

In a typical season in the United States, influenza vaccine production and distribution are largely the purview of private manufacturers and distributors. Manufacturers sell seasonal influenza vaccine directly to providers who administer vaccination, including physicians, hospitals, pharmacies, federal agencies, state and local health departments, and mass immunizers. In addition, manufacturers sell vaccine to medical supply distributors, who in turn sell it to providers and other customers. Providers administer vaccinations in a variety of locations, including physician's offices, public health clinics, nursing homes, and nonmedical locations such as workplaces and retail stores. Millions of individuals receive influenza vaccinations through mass immunization campaigns in these nonmedical locations, where organizations such as visiting nurse agencies under contract administer the vaccine. The reliance on this private-sector system affects when and how vaccine is distributed—that is, when a provider receives vaccine can depend on which manufacturer that provider ordered from and the distribution route the vaccine takes from the manufacturer to the provider. Because the influenza vaccine production process typically takes 6 or more months to complete, manufacturers must estimate the potential demand for vaccine and what their production levels will be well before the start of the season.⁷ At the end of the influenza season, any unused vaccine doses expire and therefore cannot be used in subsequent years. Accordingly, manufacturers seek to match their vaccine production to expected demand for the vaccine so that no doses remain unsold at the end of the influenza season. Manufacturers may decide to limit or stop production if they do not believe there is sufficient demand to sell all of the vaccine

⁶Each year, public health experts, including those from FDA, the World Health Organization, and CDC, study influenza virus samples and global disease patterns to identify virus strains likely to cause the most illness during the upcoming season. Based on that information and the recommendations of FDA's Vaccines and Related Biological Products Advisory Committee, FDA selects the strains for inclusion in the annual influenza vaccine for the United States. FDA has traditionally selected three strains of influenza virus—two strains of influenza type A and one strain of influenza type B—to include in the annual influenza vaccine.

⁷Influenza vaccine has generally been produced in a complex process that involves growing viruses in millions of fertilized chicken eggs. This egg-based process has been used to make vaccine in past influenza seasons, the current season, and the 2009 H1N1 pandemic.

doses they have the capacity to produce—thereby limiting the quantity produced for that season and how late in the season the vaccine is available.

Although the production and distribution of seasonal influenza vaccine is largely a private-sector endeavor, federal, state, and local governments may become more involved, particularly when there is a vaccine shortage or in the event of a pandemic. For example, during a period of vaccine shortage in the 2004–2005 season, the federal government worked with a major manufacturer and with state and local health officials to help prioritize how to distribute available vaccine to provide better access for those at high risk for influenza related complications.⁸ In the event of a pandemic, the federal government may assert more control over vaccine production and distribution than in a nonpandemic influenza season. For example, in response to the 2009 H1N1 pandemic the federal government purchased vaccine directly from manufacturers and worked with state and local governments to determine the distribution of that vaccine. In a pandemic situation when the federal government purchases all of the vaccine, the federal government can guarantee manufacturers that they will sell a certain number of doses.

⁸Of the three manufacturers of seasonal influenza vaccine for the 2004–2005 influenza season, two produced and distributed vaccine and one ceased production and did not distribute any vaccine for the U.S. market after its license was suspended by the United Kingdom in October 2004. As a result, close to half of the 100 million doses estimated for the 2004–2005 season—approximately 47 million doses—were not produced. Instead only 61 million doses were produced, of which 57 million were distributed.

**Lessons Learned on
Influenza Response
Include the
Importance of
Planning, Effective
Communication, and
the Difficulty of
Matching Vaccine
Supply with Public
Demand**

Our prior work has identified a number of lessons from the federal response to seasonal influenza vaccine shortages and the 2009 H1N1 pandemic that carry implications for future influenza seasons or another influenza pandemic. The primary lessons can be grouped into four broad, interrelated categories: the value of planning, the importance of effective communication, the difficulties in predicting all of the influenza virus strains that will be circulating in a given season, and the challenge in facilitating the matching of available influenza vaccine supply with public demand.

First, our work found that planning is critical to an effective response.

- A lesson learned from the 2004–2005 season, when there was an abrupt and unexpected loss of nearly half of the nation's expected vaccine supply, was that planning is critical to ensure timely delivery of vaccine to those who need it when demand for vaccine exceeds the available supply. That season, CDC's lack of a contingency plan contributed to delays and uncertainty about how to ensure that high-risk individuals had access to vaccine.
- We also found that planning paid off in the response to the 2009 H1N1 pandemic. For example, planning activities—including planning exercises, and interagency meetings prior to the H1N1 pandemic—built relationships that were valuable and positioned the government to respond effectively.

HHS has taken action in planning for future seasons or pandemics. For example, following the shortage of the prior season, CDC published ordering and distribution strategies for the 2005–2006 season, when there was uncertainty in vaccine production, encouraging the distribution of vaccine in multiple shipments as vaccine became available so providers could have some vaccine for their high-risk patients when vaccine was initially distributed.⁹ CDC continues to encourage this type of multiphased distribution strategy. Additionally, following the 2009 H1N1 pandemic, HHS reported that it would incorporate lessons learned from the pandemic response into its plans for responding to such incidents in

⁹See CDC, "Influenza Vaccine Prebooking and Distribution Strategies for the 2005–06 Influenza Season," *Morbidity and Mortality Weekly Report*, vol. 54, no. 12 (2005): 307–308.

the future. These included lessons that we identified, as well as other lessons HHS identified in its after-action report.

Second, our work found that clear and consistent communication—between all levels of government and with providers and the public—is key. Because the failure to effectively manage public expectations can undermine government credibility, it is essential that vaccine production efforts be paired with effective communication strategies by the federal government regarding the availability of the vaccine. The effect of communication is illustrated by past seasons:

- During the 2004–2005 season, in some instances, uncoordinated communication from federal to state and local jurisdictions, and to providers and the general public, contributed to confusion, frustration, and individuals’ failure to seek or receive an influenza vaccination.
- During the summer of 2009, HHS conveyed to state and local jurisdictions, and to the public, that a robust H1N1 vaccine supply, about 120–160 million doses, was expected to be available in October 2009. Ultimately, however, fewer than 17 million doses were shipped out that month, which did not meet the expectations of state and local governments or the public. Consequently, the public had an unfavorable view of the federal government’s ability to provide the country with the H1N1 vaccine. A Gallup survey of U.S. adults from early November 2009 found that 54 percent of adults said the federal government was doing a poor (41 percent) or very poor (13 percent) job of providing the country with adequate supplies of the vaccine.
- In our work on past influenza seasons and the 2009 H1N1 pandemic, state and local health officials emphasized the value of communication, including updating information when responding to changing circumstances, using diverse media to reach diverse audiences, and educating the public about nonpharmaceutical interventions, such as hand washing and covering coughs.

Recognizing the importance of sharing updated information, in response to problems in the past, HHS has taken steps to work with stakeholders to communicate on vaccine availability. For example, HHS’s influenza website, www.flu.gov, includes an influenza vaccine finder for individuals

seeking to find providers offering vaccination in their area.¹⁰ In addition, CDC's website has links to help health care providers find available vaccine to purchase.¹¹

While these efforts, along with regular communication and sharing of information between CDC and other stakeholders—including public health officials, providers, manufacturers, and distributors—have improved influenza-related communication, effective and consistent communication is a challenge. For example, as we reported in October 2007, one CDC official involved in communicating messages about influenza told us that it is difficult to maintain a consistent message during or between influenza seasons, because messages need to adapt to the dynamic and complex situations that constitute influenza seasons. For example, messages need to be modified to account for changes in the Advisory Committee on Immunization Practices' recommendations, which could result in the public hearing different messages before and after these revisions are made.

Third, our work found that ensuring that the annual influenza vaccine protects against the influenza virus strains that will cause serious illness for a given influenza season is difficult, because it is not possible to predict with certainty which influenza viruses will predominate that season. Traditionally, the influenza vaccines licensed by FDA for use in the United States contain three different influenza virus strains. FDA must pick which viruses to include in the vaccine many months in advance in order for vaccine to be produced and delivered on time, so there is always a possibility of a less than optimal match between circulating viruses and the virus strains in the vaccine. In recent years, the match between the viruses in the vaccine and those identified during the season has been good; however, in some seasons, this has not been the case. For example, for the 2007–2008 season's vaccine, FDA did not select the

¹⁰CDC initially created a version of the Flu Vaccine Finder to help state and local officials direct available vaccine to certain high-risk groups; this system provided state and local officials with information on where vaccine had been shipped and also allowed them to order available vaccine.

¹¹During influenza seasons when vaccine supply is challenged, the Influenza Vaccine Availability Tracking System (IVATS) becomes operational. IVATS, which is on the website of the National Influenza Vaccine Summit (www.preventinfluenza.org), enables health care providers to view at a glance which distributors have vaccine available to sell. IVATS was initiated in 2006.

influenza A virus strain that became the predominant virus in the United States that season for the vaccine, and the vaccine was not well-matched with the strains circulating in the United States that season. During a typical influenza season, including the current season, there may be two different influenza B strains circulating, or the B strain selected for inclusion in the vaccine may not be the influenza B strain that eventually circulates and causes illness. To increase the likelihood of adequate protection against circulating influenza strains, FDA approved two new vaccines that can protect against a total of four influenza strains—one more strain than traditional seasonal influenza vaccines. These new vaccines—called quadrivalent vaccines—are expected to be available for the 2013–2014 season.¹²

Finally, another lesson learned is that matching influenza vaccine supply with the public's demand is challenging, particularly as the supply of and demand for vaccine can vary throughout the season and across multiple seasons. For instance:

- While the roughly 78 million doses eventually produced for the 2000–2001 season were about the same amount produced in the previous year, a delay resulted in a shortage of vaccine during October and November when people normally receive their vaccination. During the shortage, many providers who wanted to purchase vaccine faced rapidly escalating prices from distributors with an available supply.
- For the 2003–2004 season, shortages of vaccine occurred when there was an earlier and more severe influenza season and higher than normal demand, likely resulting from media coverage of pediatric deaths associated with influenza. Manufacturers that season had produced about the same number of doses used in the previous season—about 87 million doses total—which was not adequate to meet the increased demand, according to CDC officials.
- Even in seasons when there were few licensed manufacturers or periods when demand exceeded the available supply, more doses of

¹²FDA approved MedImmune's FluMist Quadrivalent in February 2012 and GlaxoSmithKline's Fluarix Quadrivalent vaccine in December 2012 for the prevention of seasonal influenza for their intended populations. According to FDA, the approval of these quadrivalent influenza vaccines was not for a specific influenza season and the timing of the marketing launch of a new vaccine to make it available to the public is a decision made by each manufacturer.

seasonal vaccine have generally been produced than distributed, according to data from CDC, FDA, and the American Medical Association. Similarly, overall supply exceeded demand even in the 2009 H1N1 pandemic; HHS has acknowledged that the doses of H1N1 vaccine arrived too late in the response, and local health department officials told us that once the H1N1 vaccine became available, parents were not interested in vaccinating their children because H1N1 influenza vaccine activity had already peaked in their area.

The challenges in matching vaccine supply with demand in a given season are illustrated in the past two seasons. For the 2011–2012 season, manufacturers produced about 162 million doses, slightly more than the 158 million doses distributed in the prior season. However, the 2011–2012 season began late, peaked in March, and was mild compared to most previous seasons, and manufacturers were left with about 30 million doses that were produced but not distributed at the end of the season. For the current 2012–2013 season, manufacturers are expected to produce about 145 million doses. Unlike last season, CDC has reported that this season has been characterized by early and intense influenza activity throughout much of the country, and there are reports of spot shortages. Figure 2 shows the percentage of outpatient visits for influenza-like illness by month for influenza seasons in 2010–2011, 2011–2012, and 2012–2013.

Figure 2: Percentage of Outpatient Visits for Influenza-Like Illness by Month, 2010–2011, 2011–2012, and 2012–2013

Percentage of outpatient visits for influenza-like illness

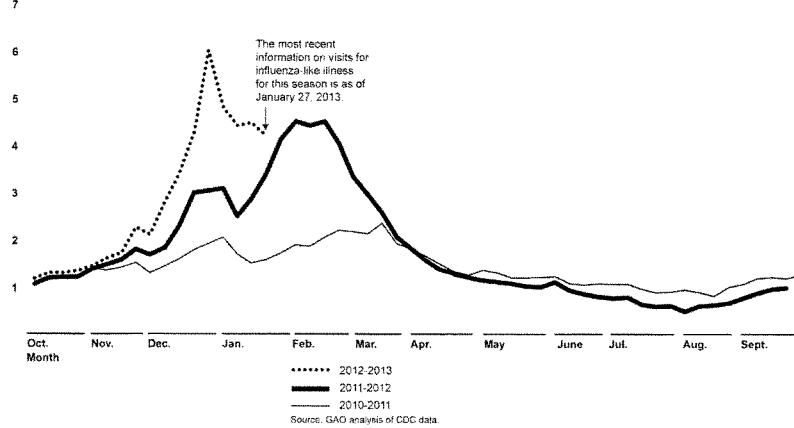
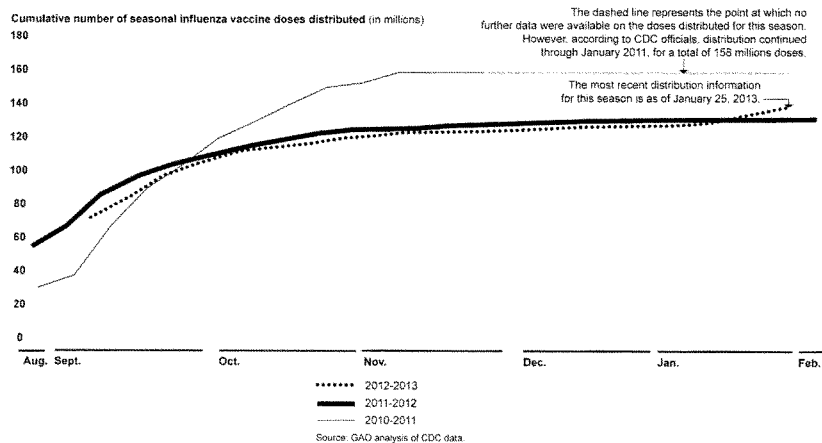


Figure 3 show the cumulative number of doses of influenza vaccine distributed by month for the same seasons.

Figure 3: Cumulative Number of Seasonal Influenza Vaccine Doses Distributed by Month, 2010–2011, 2011–2012, and 2012–2013



Recognizing the potential for a mismatch in vaccine supply and demand for vaccinations, beginning with the 2004–2005 season, CDC began purchasing a late-season influenza vaccine stockpile to provide a limited quantity of vaccine for children using federal Vaccines for Children (VFC) program funds. The purpose of this stockpile is to ensure that some vaccine would be available in the event of a late-season outbreak of influenza and related demand for vaccine.¹³ For the current season, CDC shipped about 400,000 pediatric doses of vaccines during the week of January 21, 2013, to federal depots so that 32 immunization awardees

¹³Under CDC's VFC program, vaccines are provided free of charge for certain children 18 years of age or younger, including those who are Medicaid-eligible, uninsured, or those without insurance coverage for vaccinations.

could place additional orders to protect children.¹⁴ Despite these efforts, many challenges remain. Predictions of the severity and timing of a coming seasonal outbreak, and the circulating strains, are imprecise. The vaccine production process relies on an annual manufacturing cycle that has a history of disruption. Given this production cycle, decisions must be made months in advance of a seasonal outbreak and vaccine supply orders are often placed before providers know what patient demand will be. Manufacturers may be reluctant to produce and providers may be reluctant to order vaccine that exceeds their projected demand because the product must be destroyed at the end of the season if it is not used.

HHS Has Made Investments to Strengthen the U.S. Vaccine Supply

HHS has taken steps to strengthen the U.S. influenza vaccine supply by making investments in alternative technologies—including cell-based and recombinant technologies—and enhancing domestic production capacity.¹⁵ (See app. I for additional information on these technologies). Potential threats to the egg supply such as from the H5N1 virus, in part, prompted HHS to make investments in alternative technologies for producing influenza vaccine.¹⁶ Specifically, since fiscal year 2005, HHS awarded over \$1 billion in contracts to manufacturers to develop cell-based technology.¹⁷ These contracts involved six manufacturers, and, according to HHS, established goals for manufacturers to develop cell-

¹⁴CDC reported purchasing 517,280 doses for its pediatric influenza vaccine stockpile for the 2012-2013 season. CDC reached out to immunization awardees to determine if they had the need for any additional VFC vaccine to serve VFC-eligible children in their jurisdictions. Based on this request, CDC made available approximately 400,000 doses of this stockpiled VFC vaccines to 32 immunization awardees. These doses were shipped to the federal depots serving these awardees during the week of January 21, 2013, so that the awardees could place orders.

¹⁵HHS refers to this technology as recombinant/molecular technology. According to HHS, this technology is also used for researching and developing a universal influenza vaccine. HHS's National Institutes of Health is conducting research on a universal vaccine, which it defines as a vaccine that would theoretically provide protection against any strain of influenza without needing to be updated or administered every year to protect against newly emerging annual or pandemic strains. HHS has also made other investments to enhance the U.S. vaccine supply, such as in antigen-sparing technology using adjuvants.

¹⁶In addition to human infections, strains of the H5N1 virus have infected chicken flocks and other poultry, resulting in the culling of these flocks, raising concern that the egg supply for influenza vaccine could be at risk.

¹⁷Cell-based technology has the potential to increase the overall amount of vaccine available at the end of the production process, but it does not speed up the production process itself.

based technology for influenza vaccine and obtain FDA licensure for such a vaccine.¹⁸ One of those manufacturers—Novartis Vaccines and Diagnostics, Inc. (Novartis Vaccines)—received FDA approval for its cell-based seasonal influenza vaccine, called Flucelvax, in November 2012. According to HHS, Novartis Vaccines plans to produce and distribute this vaccine for the 2013–2014 influenza season.¹⁹ (See app. II for more information on these contracts.)

In addition to investments in cell-based technology, HHS has also awarded contracts to manufacturers for the research and development of recombinant technology.²⁰ Specifically, in fiscal year 2009, HHS entered into a contract worth approximately \$81 million with Protein Sciences Corporation (Protein Sciences) for the continued development of recombinant technology for use in producing an influenza vaccine.²¹ In January 2013, FDA approved Protein Sciences's seasonal influenza vaccine made using recombinant technology, FluBlok, which will be available for the 2013–2014 influenza season.²²

HHS's investments in alternative vaccine technologies have been complemented by its investments in domestic manufacturers' production capacity. As we noted in prior work, the lack of U.S. production capacity was cause for concern among experts, in part because it is possible that countries without domestic production capacity will not have access to influenza vaccine in the event of a pandemic if countries where vaccine is produced prohibit the export of the pandemic vaccine until their own

¹⁸According to HHS, it awarded multiple contracts because it expected some attrition by manufacturers as the development of new influenza vaccines progressed.

¹⁹According to HHS, Novartis Vaccines has produced 230,000 doses of its cell-based influenza vaccine; however, none of these doses have been distributed as of February 2013.

²⁰Recombinant technology has the potential to increase the overall amount of vaccine available at the end of the production process and speed up the production process itself, in part, because unlike egg-based and cell-based technologies, it does not depend on the replication of the influenza virus for production.

²¹HHS has also made investments in the research and development of pandemic influenza vaccines using recombinant technology. See table 3 in app. II for more information on these investments.

²²According to HHS, Protein Sciences has produced 100,000 doses of its recombinant influenza vaccine; however, none of these doses have been distributed as of February 2013.

needs are met.²³ Since fiscal year 2005, HHS has made investments in enhancing domestic production capacity using egg-based technology by, for example, supporting a program to ensure a year-round, secure, domestic egg supply. Prior to this funding, manufacturers maintained a 9-month supply of eggs—enough for production only during the regular influenza season without any additional capacity for emergencies, such as an influenza pandemic. Additionally, in fiscal year 2007, HHS entered into contracts with two manufacturers for the retrofitting of existing domestic egg-based production facilities. According to HHS, the retrofitting has doubled the production capacity for one of these manufacturers and tripled the production capacity for the other. This additional capacity was used during the 2009 H1N1 pandemic to produce pandemic vaccine. Also, as a condition of receiving funding to develop cell-based technology, HHS required manufacturers to have a domestic facility where cell-based influenza vaccine can be produced. In fiscal year 2009, HHS entered into a \$486.6 million contract with Novartis Vaccines for the construction of a cell-based influenza vaccine production facility in the United States to enhance domestic production capacity. This facility was completed in November 2009 and is the facility where Novartis's Flucelvax is expected to be produced for the 2013–2014 influenza season.²⁴ These investments by HHS have contributed to the doubling of the number of domestic influenza vaccine manufacturers and a general increase in the number of influenza vaccine doses produced and distributed. (See table 1.)

²³See GAO, *Influenza Pandemic: Efforts Under Way to Address Constraints on Using Antivirals and Vaccines to Forestall a Pandemic*, GAO-08-92 (Washington, D.C.: Dec. 21, 2007). This situation occurred during the 2009 H1N1 pandemic when CSL Biotherapies in Australia and GlaxoSmithKline, plc, in Canada were required to fulfill their domestic orders for the pandemic vaccine prior to releasing vaccine to the United States.

²⁴According to HHS, Novavax Vaccines is currently producing this vaccine at its facility in Marburg, Germany.

Table 1: Number of U.S.-Licensed Manufacturers of Seasonal Influenza Vaccine and Number of Doses Produced and Distributed for the 2000–2001 through 2012–2013 Influenza Seasons

Influenza season	Number of licensed manufacturers	Total number of doses produced (in millions)	Total number of doses distributed (in millions)
2000–2001	3	78	70
2001–2002	3	88	78
2002–2003	3	95	83
2003–2004	3	87	83
2004–2005	3 ^a	61	57
2005–2006	4	92	82
2006–2007	5	121	104
2007–2008	6	141	113
2008–2009	6	143–146	111
2009–2010	6	114	114
2009 H1N1 pandemic ^b	5	186 ^c	173 ^d
2010–2011	6	168	158
2011–2012	6	162	132
2012–2013	6 ^e	145 ^f	134 ^g

Source: GAO analysis of CDC, FDA, and American Medical Association data.

Notes: Table includes the number of doses produced by manufacturers and distributed to customers, such as medical supply distributors, physicians, or other types of providers.

^aOf the three manufacturers of seasonal influenza vaccine for the 2004–05 influenza season, two produced and distributed vaccine and one ceased production and did not distribute any vaccine for the U.S. market after its license was suspended by the United Kingdom in October 2004. In addition to these three manufacturers, two foreign manufacturers' vaccines were purchased by the Department of Health and Human Services (HHS) for potential use in the United States under an investigational new drug protocol; however, none of these doses were distributed.

^bFor the 2009 H1N1 pandemic, vaccine was purchased exclusively by the federal government for distribution to state-designated locations.

^cAccording to HHS, 240 million doses of bulk pandemic vaccine was produced, of which 186 million doses were filled.

^dThis number includes doses distributed for the U.S. public, the Department of Defense, and for international response efforts.

^eThis number does not reflect FDA's most recent approvals for seasonal influenza vaccines using cell-based and recombinant technologies.

^fThis amount includes the 230,000 doses of cell-based influenza vaccine produced by Novartis Vaccines and the 100,000 doses of recombinant influenza vaccine produced by Protein Sciences. These doses of vaccine produced using alternative technologies were not distributed, according to HHS.

^gThis number is as of January 25, 2013.

Concluding Observations

Over the last decade, progress has been made in the federal government's preparation for and response to seasonal and pandemic influenza events. Planning activities have helped with response efforts, communication with the public regarding where and when to get vaccine has been clearer and more effective, and manufacturers have been encouraged to enhance domestic production capacity and develop alternative production technologies. Yet, the fact remains that when facing a typical influenza season, manufacturers must make decisions about how much vaccine to produce, providers must determine how much vaccine to order, and individuals—who may be influenced by a particular season's perceived severity and media reports—make their own decisions about whether, when, and where to seek vaccination. These disparate factors, along with challenges inherent in the vaccine production process and influenza seasons that are unpredictable in terms of duration and severity, can present barriers to successfully making desired quantities of influenza vaccine available when and where it is needed.

Chairman Murphy, Ranking Member DeGette, and Members of the Subcommittee, this completes my prepared statement. I would be pleased to respond to any questions that you may have at this time.

GAO Contact and Staff Acknowledgments

If you or your staff have any questions about this testimony, please contact me at (202) 512-7114 or crossem@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this statement. Kim Yamane, Assistant Director; Tom Conahan; Kaitlin Coffey; Cathy Hamann; and Gay Hee Lee were key contributors to this statement.

Appendix I: Influenza Vaccine Production Technologies

Traditionally, influenza vaccine—both seasonal and pandemic—has been produced using egg-based technology. However, the Food and Drug Administration (FDA) recently approved two new seasonal influenza vaccines produced using alternative technologies—one using cell-based technology and a second using recombinant technology.¹

Egg-Based Technology

Egg-based technology has been used to produce influenza vaccine—both seasonal and pandemic—for several decades. Department of Health and Human Services (HHS) officials we spoke with described it as a “tried and true” production technology with which regulators and manufacturers are familiar. This technology is used to make seasonal and pandemic influenza vaccine. This technology utilizes fertilized eggs as the medium for producing the vaccine.² Additionally, several decades of safety and efficacy data on the influenza vaccine produced using egg-based technology are available. However, the timeliness of vaccine production is hindered, in part, by egg-based technology’s reliance on seed strain development and growth. Another factor affecting the production timeline is the amount of antigen produced per egg.³ For example, during the 2009 H1N1 pandemic, vaccine delivery was delayed, in part, because of poorer yields of antigen per egg than expected. Also, the amount of influenza vaccine that can be produced depends on the manufacturer’s egg supply. It generally takes 12 to 18 months to establish an egg supply large enough to meet the demands of either seasonal or pandemic influenza.⁴

¹The Department of Health and Human Services (HHS) refers to this technology as recombinant/molecular technology. According to HHS, this technology is also used for researching and developing a universal influenza vaccine. The National Institutes of Health, which is conducting research on a universal vaccine, defines it as a vaccine that would theoretically provide protection against any strain of influenza without needing to be updated or administered every year to protect against newly emerging annual or pandemic strains.

²Producing these fertilized eggs is more difficult than producing eggs for human consumption. The fertilized eggs are typically 9 to 12 days old, and FDA requires that these eggs meet particular sanitation and other requirements.

³Antigen is the active substance in a vaccine that provides immunity by causing the body to produce protective antibodies to fight off a particular influenza strain.

⁴Since fiscal year 2005, HHS has made investments in enhancing domestic production capacity using egg-based technology by, for example, supporting a program to ensure a year-round, secure, domestic egg supply.

Cell-based Technology

The key potential benefit to cell-based technology is the ability to increase the overall amount of vaccine available at the end of the production process. This technology for influenza vaccines typically relies on the use of well-established cell lines, such as those originally derived from the kidney cells of monkeys or canines. These cells can exponentially increase in number, allowing for the rapid expansion of the medium used for influenza vaccine production. Additionally, cells can be stored in freezers and prepared for use within days or weeks for large-scale production demands. Vaccines using cell-based technology are licensed for use in the United States for use against other infectious diseases, such as polio. Despite the potential benefits of cell-based technology, there are challenges associated with its use. Similar to egg-based technology, cell-based technology relies on seed strain development and growth to obtain the influenza vaccine's antigen.

Recombinant Technology

Recombinant technology potentially increases the overall amount of vaccine available at the end of the production process and speeds up the production process itself. First, this technology can also utilize specialized cells—from mammals or from other sources, such as from bacteria, yeast, insects, or plants—that can exponentially increase in number as the medium for influenza vaccine production, allowing for the rapid expansion of the medium used for influenza vaccine production. Recombinant technology also has the potential to speed up the production process because it does not rely on the development and growth of a seed strain to obtain the influenza vaccine's antigen. Instead, antigen is derived from the protein(s) on the surface of the influenza virus or from the virus's genes. Recombinant technology is currently used in U.S.-marketed vaccines against other diseases, such as hepatitis B and the human papillomavirus, so FDA has experience reviewing licensing applications for vaccines produced using this technology.

Appendix II: HHS's Contracts for the Research and Development of Cell-Based and Recombinant Influenza Vaccines

Table 2: HHS Contracts Awarded for Research and Development of Cell-Based Influenza Vaccine

Manufacturer	Fiscal year of award	Total obligations (dollars in millions) ^a	Development status as of February 2013			
			Vaccine approved	Application pending	Vaccine in development	Contract no longer active
sanofi pasteur ^b	2005	\$77.0 ^c				X ^d
GlaxoSmithKline	2006	274.8			X	
Novartis Vaccines	2006	220.5	X ^e			
DynPort/Baxter ^f	2006	242.3 ^g		X ^h		
MedImmune, LLC	2006	169.5				X ⁱ
Solvay Pharmaceuticals ^j	2006	48.6 ^k				X ⁱ
Total		\$1032.7				

Source: GAO analysis of HHS and manufacturer data.

Notes: HHS data are as of February 2013, while manufacturer data are as of June 2011.

^aObligations are definite commitments that establish the legal liability of a federal agency to make payments for goods or services ordered or received, immediately or in the future. Because payments are typically made as goods or services are received, the funds listed may not have been expended. Upon termination of a contract, unexpended funds may be deobligated and, depending on the terms of their appropriation, may remain available to the agency.

^bThe policy of sanofi pasteur is to spell its name without capital letters.

^cThis amount reflects a \$20 million deobligation in fiscal year 2009. A deobligation refers to the cancellation or downward adjustment of previously incurred obligations.

^dThe manufacturer concluded that cell-based technology was not more advantageous than egg-based technology and lacked a clear path for further development, and thus the manufacturer chose to forgo pursuit of cell-based technology. According to HHS, the department terminated this contract for the development of a cell-based influenza vaccine in fiscal year 2009.

^eThis vaccine, Flucelvax, was approved by FDA in November 2012 and is expected to be available during the 2013–14 influenza season.

^fHHS contracted with DynPort Vaccine Company LLC (DynPort), which collaborated with Baxter International Inc., (Baxter) to develop a seasonal and a pandemic influenza vaccine using cell-based technology. Baxter oversaw the development of the vaccine, including supporting licensure efforts for the seasonal vaccine. Baxter also oversaw the completion of clinical trials for the pandemic vaccine. DynPort managed the overall project as well as clinical trials. For the purposes of this statement, we refer to this contract as DynPort/Baxter because of the collaboration between the two manufacturers.

^gThis amount includes a modification of \$201.3 million made in fiscal year 2007 to the existing contract. The original contract was awarded for \$41 million.

^hAccording to HHS, DynPort/Baxter anticipates submitting a licensing application to FDA in 2013.

ⁱAccording to HHS, a stop-work order was issued in fiscal year 2010 and discussions related to the termination of this contract are ongoing, as of February 2013.

^jAbbott Laboratories purchased Solvay Pharmaceuticals in February 2010.

^kThis amount reflects a \$250 million deobligation in fiscal year 2009.

^lThe manufacturer discontinued plans for the construction of a cell-based influenza vaccine production facility in the United States because of lack of commercial viability. HHS terminated this contract for the development of a cell-based influenza vaccine in June 2009.

Appendix II: HHS's Contracts for the Research
and Development of Cell-Based and
Recombinant Influenza Vaccines

Table 3: HHS Contracts Awarded for Research and Development of Recombinant Influenza Vaccine

Manufacturer	Fiscal year of award	Total obligations (dollars in millions) ^a	Development status as of February 2013			
			Vaccine approved	Application pending	Vaccine in development	Contract no longer active
Protein Sciences ^b	2009	\$81.3	X ^c			
Novavax ^d	2011	97.3			X	
VaxInnate ^d	2011	117.9			X	
Total		\$296.5				

Source: GAO analysis of HHS data.

^aObligations are definite commitments that establish the legal liability of a federal agency to make payments for goods or services ordered or received, immediately or in the future. Because payments are typically made as goods or services are received, the funds listed may not have been expended. Upon termination of a contract, unexpended funds may be deobligated and, depending on the terms of their appropriation, may remain available to the agency.

^bAccording to HHS, this contract requires Protein Sciences to establish enough domestic manufacturing capacity to provide finished vaccine within 12 weeks of the beginning of a pandemic and to produce at least 50 million doses of pandemic vaccine within 6 months of the beginning of a pandemic.

^cThis vaccine, FluBlok, was approved by FDA in January 2013 and is expected to be available during the 2013–2014 influenza season.

^dAccording to HHS, this manufacturer is currently conducting clinical trials for its recombinant pandemic influenza vaccine.

Related GAO Products

Influenza Pandemic: Lessons from the H1N1 Pandemic Should Be Incorporated into Future Planning. GAO-11-632. Washington, D.C.: June 27, 2011.

Influenza Vaccine: Federal Investments in Alternative Technologies and Challenges to Development and Licensure. GAO-11-435. Washington, D.C.: June 27, 2011.

Influenza Pandemic: Monitoring and Assessing the Status of the National Pandemic Implementation Plan Needs Improvement. GAO-10-73. Washington, D.C.: November 24, 2009.

Influenza Pandemic: Gaps in Pandemic Planning and Preparedness Need to Be Addressed. GAO-09-909T. Washington, D.C.: July 29, 2009.

Influenza Pandemic: Continued Focus on the Nation's Planning and Preparedness Efforts Remains Essential. GAO-09-760T. Washington, D.C.: June 3, 2009.

Influenza Pandemic: Sustaining Focus on the Nation's Planning and Preparedness Efforts. GAO-09-334. Washington, D.C.: February 26, 2009.

Influenza Pandemic: HHS Needs to Continue Its Actions and Finalize Guidance for Pharmaceutical Interventions. GAO-08-671. Washington, D.C.: September 30, 2008.

Influenza Pandemic: Efforts Under Way to Address Constraints on Using Antivirals and Vaccines to Forestall a Pandemic. GAO-08-92. Washington, D.C.: December 21, 2007.

Influenza Vaccine: Issues Related to Production, Distribution, and Public Health Messages. GAO-08-27. Washington, D.C.: October 31, 2007.

Influenza Pandemic: Further Efforts Are Needed to Ensure Clearer Federal Leadership Roles and an Effective National Strategy. GAO-07-781. Washington, D.C.: August 14, 2007.

Influenza Pandemic: Efforts to Forestall Onset Are Under Way; Identifying Countries at Greatest Risk Entails Challenges. GAO-07-604. Washington, D.C.: June 20, 2007.

Related GAO Products

Influenza Pandemic: DOD Combatant Commands' Preparedness Efforts Could Benefit from More Clearly Defined Roles, Resources, and Risk Mitigation. GAO-07-696. Washington, D.C.: June 20, 2007.

Influenza Pandemic: Applying Lessons Learned from the 2004–05 Influenza Vaccine Shortage. GAO-06-221T. Washington, D.C.: November 4, 2005.

Influenza Vaccine: Shortages in 2004–05 Season Underscore Need for Better Preparation. GAO-05-984. Washington, D.C.: September 30, 2005.

Influenza Pandemic: Challenges in Preparedness and Response. GAO-05-863T. Washington, D.C.: June 30, 2005.

Influenza Pandemic: Challenges Remain in Preparedness. GAO-05-760T. Washington, D.C.: May 26, 2005.

Flu Vaccine: Recent Supply Shortages Underscore Ongoing Challenges. GAO-05-177T. Washington, D.C.: November 18, 2004.

Infectious Disease Preparedness: Federal Challenges in Responding to Influenza Outbreaks. GAO-04-1100T. Washington, D.C.: September 28, 2004.

Flu Vaccine: Steps Are Needed to Better Prepare for Possible Future Shortages. GAO-01-786T. Washington, D.C.: May 30, 2001.

Flu Vaccine: Supply Problems Heighten Need to Ensure Access for High-Risk People. GAO-01-624. Washington, D.C.: May 15, 2001.

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Mr. MURPHY. Thank you, Dr. Crosse, and thank you to all the panelists here. Every member will have 5 minutes to ask some questions. At this point the Chair recognizes himself for 5 minutes.

Dr. Frieden, the Centers for Disease Control recommends every American over the age of 6 months get a vaccine. I believe it is less than 50 percent of Americans actually get immunized. First of all, what is the optimal percentage that you hope for, for example, the herd effect, for people to get immunized?

Dr. FRIEDEN. We like to see at least 80 percent vaccination rates and obviously higher is better.

Mr. MURPHY. So why aren't more people getting vaccinated?

Dr. FRIEDEN. What we find is that the easier you make it for people, the more likely they are to be vaccinated. One encouraging trend in recent years is that an increasing proportion of all vaccinations are being given in workplaces and in pharmacies. In fact, more than a third of vaccines so far this season have been given in either of those settings for adults. We also find that the health care system can make a big difference, so things like standing orders or routinely providing it to all people who come into emergency departments, having subspecialists who see patients also recommend vaccination and arrange it, either at a pharmacy or elsewhere, standing orders, reducing barriers, eliminating cost sharing, which is something that is expanding to the private insurance market through some of the provisions of the Affordable Care Act and also education. Hearings like this, community outreach, public education all makes a difference.

What we found this year as an example is in the one group, pregnant women, we have looked very closely at and what we find is that if the obstetrician actually provides flu vaccine in the office, we have about a 75 percent vaccination rate among pregnant women whereas overall it is at about 50 percent. That is actually a big increase from previous years. There was a bump during the 2009–2010 pandemic, and that has been sustained.

The second group that we have looked at closely is health care workers because when someone is vaccinated, they not only protect themselves, they protect those who they have contact with, and we know that there is some evidence that suggests that low vaccination in health care workers in nursing homes in particular can have very severe ramifications. What we find is that pharmacists, nurses and doctors have vaccination rates of 80 to 90 percent, so quite good, but that allied health workers and people who work in nursing homes may be under 50 percent, so we have identified the areas where we need to reach out more. The bottom line is, fewer barriers, more convenience makes a big difference.

Mr. MURPHY. I am just curious because you say that about the barriers with cost sharing. Have you done any follow-up studies? For example, you mentioned a pharmacy or somewhere else might provide these vaccines. I mean, I have seen some for free, some for extremely lost cost. Have you done any correlational studies to help understand that part?

Dr. FRIEDEN. I am not familiar with whether we have done this in influenza. This has been looked at in a variety of programs and it is pretty consistent, that cost sharing reduces utilization, but we

can get back to you to see if that has been looked at in influenza specifically.

Mr. MURPHY. And just a quick myth check. When a pregnant woman gets a vaccine, is that any risk to her child?

Dr. FRIEDEN. No, there is not. We recommended the inactivated vaccine for pregnant women rather than the live, attenuated vaccine.

Mr. MURPHY. Thank you. Now, we know it has been particularly hard on seniors, so Dr. Frieden and Dr. Goodman, why has this been the case for seniors this year?

Dr. FRIEDEN. H3, for reasons that we don't fully understand, years that are H3 predominant, and this season is overwhelmingly H3 predominant, tend to be more severe among the elderly. There are various theories for that but bottom line, is we are not sure why. It is something that we see in 2003–2004 as well as 2007–2008. Those were our two prior H3-predominant seasons and similarly in those years the disease is more severe among the elderly. That is one of the reasons we try to vaccinate around the elderly so that we can reduce spread in the population, and we encourage prompt treatment because treatment particularly in the first 48 hours can improve outcomes.

Mr. MURPHY. Dr. Goodman, let me add a little part to that too. Can you speak to any recent innovations in vaccine technology that can lead to more effectiveness for seniors?

Dr. GOODMAN. Well, I think this is a big challenge, and part of the challenge is inherently related to the answer to your last question to Dr. Frieden, which is that we don't respond that well even to the virus itself. This is why we get so sick and why so many infections end up doing badly. Part of the problem is that when you give the same material that is in the virus in the vaccine, we don't always respond that well to that either. There are a number of approaches being taken to potentially enhance the immune response, and most of these are in the research and development stage. Some are being supported through HHS and NIH funding. For example, if you package the proteins of a virus in a particle that appears or the immune system sees as a virus, sometimes called a virus-like particle, that can sometimes induce a stronger immune response. The use of adjuvants or substances that boost the immune response can give a stronger immune response. So these things are all being examined and they need thorough examination for safety and effectiveness.

There are also parts of the virus that have been discovered recently. For example, something called the stalk is part of the protein we immunize against but it is not normally in the vaccine. Yet, it seems to be conserved year after year in multiple isolates. Therefore, if we can induce a good immune response against that, it would help.

I want to take one opportunity to add to Tom's response on your comment about pregnancy.

Mr. MURPHY. If you can do it quickly. I am out of time.

Dr. GOODMAN. Yes, because I think one of the ways we can increase uptake of vaccines for people is for them to better understand the science. There was recently published a study in Norway that showed in 115,000 women who received influenza vaccine,

their fetal outcomes were, if anything, better than people who hadn't received vaccine. The study showed that a significant reduction in influenza disease was associated with vaccine use. So, the science is there to support the safety of the vaccine in pregnant women.

Mr. MURPHY. Thank you. I am out of time. I will now recognize Ms. DeGette for 5 minutes.

Ms. DEGETTE. Thank you very much, Mr. Chairman.

First of all, to the panel, this is encouraging news and I am glad to hear it after the number of hearings we have. Dr. Crosse, you talked about a number of advancements that we have made and also the challenges that we are facing. I am wondering if you can just briefly tell me about intergovernmental cooperation in identifying potential pandemics and communication. Has that also improved?

Ms. CROSSE. That has improved. CDC's global surveillance has improved significantly in the last decade, and as we know, many of these strains emerge somewhere else in the world. In fact, people were surprised that the H1N1 emerged in North America.

Ms. DEGETTE. But has that communication improved?

Ms. CROSSE. It has improved. Across the board, we are in much better shape than we were 10 or 12 years ago.

Ms. DEGETTE. That is great.

Ms. CROSSE. There is still room for improvement.

Ms. DEGETTE. Sure, and what about surge capacity? That was the other thing we have always been concerned about.

Ms. CROSSE. Surge capacity remains a significant challenge. Emergency rooms every winter are flooded with patients who are sick with, as we saw this winter, influenza, norovirus, other kinds of infectious diseases and, you know, that capacity has not significantly changed.

Ms. DEGETTE. And Dr. Frieden, is this something we are working on? Yes or no.

Dr. FRIEDEN. Absolutely.

Ms. DEGETTE. Thanks. If you can supplement and let me know what you are doing, that would be great.

Dr. Goodman, I wanted to ask you, Dr. Crosse had said that these new types of vaccines, the non-egg-based ones, are coming into production for next season. Is that right?

Dr. GOODMAN. Well, they have both been licensed and both manufacturers have stated they intend to produce the vaccine.

Ms. DEGETTE. OK. And what about some of these methods for increasing the effectiveness? Are those also coming online quickly?

Dr. GOODMAN. There we are talking about that they are in active research and development. However, as you know, even for a promising technology now being looked at in research that looks good, that will be several years at least.

Ms. DEGETTE. OK. So that is several years, but the other ones are coming online?

Dr. FRIEDEN. Yes.

Ms. DEGETTE. Now, what would happen if we had an avian flu pandemic or something? Would we be able to make vaccines more quickly than we can now?

Dr. GOODMAN. Well, we are definitely better prepared in a number of ways.

Ms. DEGETTE. I am sorry. I only have 5 minutes. So would we be able to make a large number of vaccines more quickly now with these new techniques, say in the next couple of years?

Dr. GOODMAN. Yes. Between the new techniques and the increased capacity, yes, but we have a way to go.

Ms. DEGETTE. Yes. So now I want to ask you a question in that direction which, as you know, next month we are supposed to have this sequester hit, and under the sequester, non-defense discretionary spending is going to be cut across the board by 5.2 percent. So I am wondering, maybe Dr. Frieden, Dr. Crosse and Dr. Goodman, if you can talk to me about what this would do for operations at the FDA and CDC, both in terms of the research that is going on and also in terms of the preparedness. If we put a 5.2 percent cut immediately, what would this do to our ability to do all these preparations? Why don't we start with you, Dr. Frieden?

Dr. FRIEDEN. Well, the threats to our health and influenza are not reduced by 5 percent, so if we have fewer resources, we have to do everything we can to limit the harm that that would do, and we are focusing on efficiencies. We have already eliminated substantial administrative costs, but more than two-thirds of our funding goes out to State and local health departments, and while we would try to protect the front lines, there would be no alternative but to reduce funding there—

Ms. DEGETTE. So you would have to reduce funding in the short term but also I would assume you would have to reduce funding as you are working towards increasing surge capacity and communication and interoperability and all of that, right?

Dr. FRIEDEN. With fewer resources, we would have less capacity to detect, respond and develop better tools in the future.

Ms. DEGETTE. What about your agency, Dr. Goodman?

Dr. GOODMAN. Well, a substantial cut would have effects, and we certainly hope we are able to avoid that. It would affect, for example, the work we are doing to try to provide science and highly interactive review processes with development of these new technologies. It also affects FDA's user fees program, so that would potentially have some effects on review process, but we are hoping this can be avoided.

Ms. DEGETTE. And Dr. Crosse? And maybe you can also talk to the NIH since we don't have an NIH person here.

Ms. CROSSE. Well, I am afraid I don't know how HHS plans to implement any sequester and whether or not they are going to take money across the board or from particular pockets.

Ms. DEGETTE. OK. Thank you. Thank you, Mr. Chairman.

Mr. MURPHY. Thank you. I now recognize the vice chairman of the committee, Dr. Burgess from Texas.

Mr. BURGESS. Thank you, Mr. Chairman.

I actually wasn't going to pursue this line of questioning but since it has already been broached, I mean, any of us who are charged with running a small business or a large agency understand that from time to time we are going to have to make adjustments, and part of our role as leaders in whether it be a small business, a medical practice or the CDC or the FDA, you have to

be able to look at those things that you do within your agency or your organization and decide how to prioritize, and I just—you know, a 5 percent cut, did I ever have to deal with that in my medical practice? You bet I did, and I had to go through every line in the budget and decide what is mission critical and what is not. I don't think that you all are any less capable of doing that, and certainly my goal in the past had been to get the Department of Health and Human Services in here and talk about this last year. There seems to be an unwillingness to do that. But just from where I sit, I think if you are not already doing that within your agencies and organizations, I would encourage you to do so because this may very well be the reality and the question is not will a sequester go through but how many will you face over the next several years. So I just felt obligated to make that editorial statement. Again, it wasn't part of our hearing agenda today. It is too bad we haven't had anyone from HHS or Office of the Management and Budget come in and talk to us about their plans, and I think that certainly affects the governance of this committee but it also affects your role and your lives on a daily basis.

Now, it is unfortunate that the National Institute of Health is not here because Dr. Goodman, you were asked a question about how quickly can you do some of these things, and I just remember the experience of 2009 and the H1N1, and probably one of the scariest conference calls I have ever been on was in the middle of the NBA playoffs, or I guess it was the NCAA playoffs when these kids were coming back from Mexico with this novel influenza, and all of the things we had been warned out with the avian flu, H5N1, seemed to becoming true very quickly with this new strain. Now, it didn't turn out to be as devastating as that afternoon painted but when young populations are predominantly being affected, there seems to be the facility of transfer from human to human seemed to be well established, and the overwhelming immune response from a younger person being very detrimental to their health. I mean, these were all things we had been warned by Secretary Leavitt in the previous Administration and now they were coming true literally before our eyes. And yet you all, CDC, FDA, NIH worked together, and by August there were preparations for having this vaccination available for schoolteachers when school started the next month, and I thought that was an incredible accomplishment. I am old enough to remember the last swine flu epidemic when the complications of the vaccination were worse than the illness, so I was gratified that all parts seemed to work together. I am sure both of you were there at that time. Are you as good now as you were 4 years ago or maybe even a little bit better now? Dr. Frieden, we will take you first.

Dr. FRIEDEN. I think we have continued to make progress. I do think a lot of the H1N1 pandemic experience is important to understand and learn from it as the GAO has summarized. You know, H1N1 was not a mild pandemic. About 60 million Americans got sick, more than a quarter of a million were hospitalized, more than 12,000 died including more than 1,200 children, and the tragedies that you referred to earlier are heartbreaking. So we do everything we can to maximize use of existing tools. There were more than 88 million doses of vaccine administered. We shipped vaccine to more

than 70,000 sites and more than 300,000 shipments generally the day after it was approved for shipping, and we think that both vaccination and treatment prevented around a million cases, roughly 15,000 hospitalizations, hundreds of deaths and tens of millions of dollars of health care costs. So I do think there is a lot that went well in that but there is always things that we can do better, and coming up with a vaccine that we can develop faster, get to market faster, extending our global surveillance.

So no one expected a pandemic to emerge in North America, and we had been focusing in places where pandemics generally emerge, in Asia, but we need to continue to develop our surveillance. There is so much we don't know about influenza around the world, what the seasonality is, what the predominant strains are, what the burden is, so we are working very closely with global partners around the world, and that is a very important part of protecting those countries and protecting ourselves, and then finally of strengthening the vaccine production systems.

Mr. BURGESS. Well, you know, I am about of time, but this committee so often focuses on what didn't go right. I think from time to time we need to focus on what has gone right, and certainly the experience with H1N1, and I only look to improvement from that, but there were a lot of positives to take away from that experience.

I will yield back, Mr. Chairman.

Mr. MURPHY. I thank the gentleman. Next is Mr. Green of Texas. You are recognized for 5 minutes.

Mr. GREEN. I thank our panel and appreciate your patience. I talked earlier to Dr. Frieden. I think the flu epidemic that we had—and I watched your map, and being in Texas, at least for most of the Christmas holidays, I saw it happening there.

I guess some of the questions that I have for the panel, Dr. Frieden, how can public health providers and hospitals and hospitals and patients, what can we do to reduce the burden of the surge of the patients in our health care facilities during a bad flu season? I know our emergency rooms are stacked up. You know, typically you can't do a whole lot about it except the vaccination, which gets into my other question. How can we actually do more than we are doing now to increase the percentage of people who are getting their flu shot in September instead of waiting until the end of December or January?

Dr. FRIEDEN. Thank you very much. In terms of the surge, we have worked very closely with the Assistant Secretary for Preparedness and Response, and we have actually unified two different federally funded programs. One is the preparedness program, the Public Health Emergency Preparedness program, and the second is the Hospital Preparedness program. We now have a common application, common system, and that makes it much easier for State and localities to use federal dollars to improve their ability to address surge capacity. We have also seen some creative approaches in different States where nurse call lines have been used through private insurers, through HMOs, through private doctors to talk to patients and for the routine patients to address their needs over the phone, perhaps prescribe medications for them if needed, tell them when they need to come in and when they don't need to come in.

We also look at what we would do in a surge. It is bad enough if an emergency department is getting so many patients in, but if we have a very severe pandemic, some of the things that would be really problematic is the ability to provide emergency ventilation, to breathe for patients who can't breathe for themselves, so through the strategic national stockpile, we have been increasing the availability of practical, effective respirators, and in fact, BARDA has come up with some new designs that should be on the market next year, which are very encouraging, low cost, high quality, easy to roll out, because this would be the lowest common denominator. This would be the bottleneck in an emergency, or one of them, is being able to help people breathe for a period of time until they get better.

In terms of increasing vaccination rates, I think what we have learned is, make as many options as possible so people can get vaccinated at school, at work, at pharmacies, but within the health care system make it is automatic as possible so that all too often people do go to the doctor but they don't get the vaccination. The strongest risk factor for not being vaccinated is the doctor didn't offer it or recommend it or provide it, so we want to have automatic systems to increase vaccination rates.

Mr. GREEN. Did the Affordable Care Act help on that in providing vaccinations more readily available?

Dr. FRIEDEN. One of the components is that for private insurers, it requires no copayment for a vaccination.

Mr. GREEN. For either Dr. Frieden or Dr. Goodman, are we seeing resistance to Tamiflu?

Dr. FRIEDEN. We have seen virtually no Tamiflu resistance this season in the circulating strains.

Mr. GREEN. Outstanding. And again, the vaccination rate, I know making is more available, and I know the controversy over even medical facilities saying we are going to require all our staff to have the influenza vaccination. In the private sector, I have companies that are doing that for their employees just because it makes good business sense. What we are seeing on that? Is there a lot of resistance from folks even in the health care sector saying we don't want to take the vaccine?

Dr. FRIEDEN. I think the biggest lesson is making it easy and accessible. So 80 to 90 percent of pharmacists, doctors and nurses are getting vaccinated, but among allied health workers who may not be able to get vaccinated readily and in nursing homes which may not be doing as good a job as vaccinating, rates are 50 percent or lower.

Mr. GREEN. And in nursing homes, you have immune-challenged patients. You have the elderly. It is almost like it would be an incubator for it.

Dr. FRIEDEN. And nursing homes are particularly important to increase vaccination rates because there is some evidence that the residents of nursing homes do worse when the staff don't get vaccinated.

Mr. GREEN. Thank you, Mr. Chairman.

Mr. MURPHY. I thank the gentleman for yielding back. I now turn to the gentleman from Georgia, Dr. Gingrey.

Dr. GINGREY. Mr. Chairman, thank you, and witnesses, I apologize for coming in late, and I may end up asking you questions obviously that have already been asked. Just forgive me for that, and maybe if you repeat it, it will stick in all of our brains better anyway.

Dr. Frieden, I thought I would ask you the first question. According to your Web site, the CDC Web site, and in your written testimony, manufacturers have produced 145 million doses of flu vaccine this season and have distributed roughly 135 million, which is almost 2 million more doses than last year. Why then do you think this season has been more severe despite the increase in the vaccine compliance? More folks are getting the flu vaccine, and I am one. I didn't get the flu, thank goodness, but a lot of folks did.

Dr. FRIEDEN. This year's flu is H3N2, and seasons that are predominant for H3N2, the particular strain of flu, tend to be more severe. This year is quite predominant of H3N2. The last two seasons that happened were 2003–2004 and 2007–2008, and in both of those years they were severe flu seasons, particularly for the elderly.

Dr. GINGREY. Were they also H3N2?

Dr. FRIEDEN. They were. And why H3 is more severe, there are some interesting theories but we do not know for certain. We do know that our vaccine efficacy, our early season estimate was about 60 percent overall. We also know that in previous years, generally the elderly tend to be less protected by the flu vaccine than the non-elderly and the frail elderly even less so. We are only at around 40 percent overall vaccination rates, so being able to knock down influenza by vaccinating lots of people will probably require more vaccination than we are seeing but, you know, a reduction of 60 percent in medically attended flu from vaccination also probably means significant reduction in the spread of flu from those people who get vaccinated.

Dr. GINGREY. And also I guess maybe decreased severity of the infection, that they do better than had they not had the shot obviously.

Dr. Goodman, I noticed that there was a lot of discussion about the process of cell-based or egg-based growth factor in vaccine production. I remember all that discussion several years ago when we had that avian flu outbreak and the great concern there. How close are we to developing what you would call a universal flu vaccine?

Dr. GOODMAN. I think if you had asked me a couple of years ago, I would say we really can't be that optimistic. It's sort of a holy grail. I think there have been some scientific leads in the last 2 or 3 years that are a little more promising, and if some of these pan out, I mentioned a couple of possible technologies—directing the vaccine at conserved parts of the virus. It is possible that we could at least have some real leads and progress in this direction in the next 5 to 10 years but it is not something that is just around the horizon.

The good news is that the science that is out there to understand the immune system and understand the virus now is extraordinary, and we are all beginning to work to put that together, but we have a way to go.

Dr. GINGREY. Dr. Goodman, thank you.

And Dr. Crosse, in your testimony you stated that since 2005 Health and Human Services had awarded over a billion dollars in contracts to six different manufacturers who are developing the cell-based technology to enhance our domestic vaccine production capacity, and I am sure that that is a good thing. Yet only one of those manufacturers, Novartis, has received the FDA approval for vaccine production in the 2013–14 season. Is the FDA continuing to work with the five other manufacturers to continue its progress on switching to a faster and a more economic production model? I know I could have asked Dr. Goodman this exact same question but if you will?

Ms. CROSSE. We understand that of the six, there are—in addition to the one vaccine that has just been licensed, there are two more that are in later stages of clinical trials and that may be able to complete the process and be licensed in the next year or two. I can't really predict how quickly they may come along. The other three, they have ceased activities. I believe two of those contracts have already been canceled.

Dr. GINGREY. Who are the names, Dr. Crosse or Dr. Goodman, if you know, that are working on this cell-based—

Mr. MURPHY. Is that something you can get back to the committee?

Dr. GOODMAN. What I would say is, those who are actively working on new influenza vaccine technologies, yes, we are working in a highly interactive way with them and with BARDA and HHS to help make that happen. The intent—some of these went through a process where in essence the most promising technologies and the things that have proceeded the fastest are the ones that are continuing to be funded, and others have dropped out of the process.

Dr. GINGREY. Thank you all, and Dr. Crosse. I think the chairman is gonging me. He has the shepherd's hook out. Mr. Chairman, thank you for your patience. I know I went over a bit. I yield back.

Ms. CROSSE. There is a table in my statement that has it.

Mr. MURPHY. That is part of the record. Thank you, Dr. Gingrey. The Chair now recognizes the gentleman from New Mexico, and welcome to the committee, Mr. Lujan.

Mr. LUJAN. Mr. Chairman, thank you very much. I really appreciate that. And to the witnesses, thank you for your testimony and for being here today.

A different kind of a question. A critical piece of this infrastructure is the National Infrastructure Simulation and Analysis Center, or NISAC, which is a project, a program that exists at both Los Alamos and Sandia National Laboratories. NISAC has the capability to model global spread of flu strains and has done so in the past. Have you engaged the national security laboratories to use their predictive modeling capabilities such as NISAC to understand both the spread of influenza as well as to devise strategies for interdiction?

Dr. FRIEDEN. We have had some interactions with them. I would have to get back to you with the details of those, but certainly the advanced computing is quite important including in some of the new diagnostic and genomic experiences. What we are able to do now is to sequence entire genomes in just a few hours and to put

that together is like putting together a jigsaw puzzle with more than a million pieces. So the computing power needed for that is quite important, and that is an area where we have collaborated with the national labs and where we see potential for future growth.

Mr. LUJAN. Thank you. Anyone else? I would really encourage that we try to work with our departments, agencies to encourage them to closely work with the national labs in this endeavor. There is a huge benefit, and we saw that the last time that we had a pandemic break out.

My State is also home to a large population of Native Americans like other communities across the country as well as a diverse population. What are your agencies doing to ensure that these communities are being reached out to and included in your priorities when it comes to pandemic flu preparations, and is there active consultation?

Dr. FRIEDEN. In fact, just last week, we had our tribal consultation advisory committee meeting at CDC in Atlanta. We worked very closely with Native American groups. As you know, during the 2009 pandemic, we identified Native Americans as one group that was more severely impacted by influenza for reasons that we don't fully understand. We have for many years had a very productive relationship with the tribes on immunization issues, and vaccine uptake tends to be high in many of the tribes. In fact, we have collaborated with tribal leaders and tribal members to do some very important research on things like pneumococcal disease in the tribes, and that research benefited not only the tribes but the population throughout the United States and throughout the world. So there is a good collaboration, good consultation. We have explored ways to reach out and increase vaccination rates. We have also worked closely with the Indian Health Service on detection response and vaccination not only in influenza but other infectious and non-infectious diseases. For example, we recently identified spread in New Mexico of the Rocky Mountain spotted fever from one reservation to another through the dog tick, and we are working with private industry and tribal leaders to control that disease with some efficacy and impact. So we have a real focus on working effectively with higher-risk groups including Native Americans and Alaska Natives.

Mr. LUJAN. I appreciate that very much and I look forward to learning more about that.

One of the questions that has been asked over and over is, why aren't people taking the vaccine. We know that education is important as well. Are there a lot of efforts being put behind addressing mistruths or misconceptions associated with getting the flu shot and what impacts to each of you might sequestration have associated with scale-backs that we have seen with disease surveillance activities or some of the work that takes place from an education perspective?

Dr. FRIEDEN. In terms of your first question, increasing uptake we think is going to require efforts on many fronts, making vaccine easier for people to take, making it part of the work flow of health care professionals. Too many people do see a doctor during flu season but don't get vaccinated. Increasing the options for vaccination,

and sunlight is the best disinfectant, so providing information. There are people who have some reluctance about vaccination and just providing the information openly we find to be the best way. We are completely open to all of the adverse events that people report after vaccination are all reported on our Web. We provide information openly so if there are any concerns, they can be addressed.

As I noted earlier, we have made substantial administrative savings at CDC in recent years through travel conferences, leases, BlackBerrys, printers, computers, and we have been able to reduce administrative expenses but at this point further reductions will unfortunately translate into reductions in support that we provide for tribes, for States for localities for disease prevention and control as well as for core activities.

Mr. LUJAN. Thank you, Chairman. I yield back.

Mr. MURPHY. I thank the gentleman for yielding back. I now recognize another new member to the subcommittee, the gentleman from Mississippi, Mr. Harper.

Mr. HARPER. Thank you, Mr. Chairman, and thank each of you for being here, and I appreciate the work you do. It is extremely important, and we certainly want to make sure that you are equipped to do that job in an effective way.

You know, I hadn't planned on touching on this, but since it has come up and continues to come up about the sequestration and the potential 5.2 percent cut, I just want to make sure that—and Dr. Crosse, you gave an answer that was—I will leave you alone because you said you didn't know, so you can take a little break on this one. But Dr. Frieden and Dr. Goodman, you both indicated that it could impact actual programs to go out. It would seem to me, I want to make sure that you are not saying how that would be done or how you would operate within that, but it would seem to me if you got 94.8 percent of your budget, that you can work it out internally and administratively where that wouldn't have an impact on patient care or on the folks that you would be reaching, and I want to make sure that I am not reading something into your statements as to what you said because I know built into a budget you have open positions that may not need to be filled, you have administrative costs—it may be travel, it may be advertising, it may things that you built in that you wanted to do that perhaps you can trim back but won't have a direct impact if this does indeed kick in. And Dr. Frieden, I will let you go and then Dr. Goodman next.

Dr. FRIEDEN. We do take very seriously being diligent stewards of the funds entrusted to us, and over the past few years as we have seen some reductions in recent years, we have gotten out of leases, we have reduced conferences, consulting contracts. We actually at a flat budget level sent more money out to the field. So we feel that we have done, I can't say absolutely everything we can do but we have certainly done a great deal of what we can do.

Mr. HARPER. But it is fair to say, Dr. Frieden, I know we have limited time here but it is fair to say you would make every effort you could and within the organization to make sure that it didn't have that impact, if at all possible? That would be a fair statement, wouldn't it?

Dr. FRIEDEN. We would certainly do everything we could to mitigate the negative health consequences.

Mr. HARPER. Dr. Goodman?

Dr. GOODMAN. Yes, I think I have a very similar response in that we have tried to tighten things up and be efficient stewards of our resources and have our resources really have the public health benefit that you and the American people want us to provide so we are doing that. If we were faced with a cut, it would have some consequences but certainly we are going to manage that in the most responsible way that we can.

Mr. HARPER. Fair enough. Thank you, Dr. Goodman and Dr. Friedman, for those answers.

You know, we are obviously concerned about the influenza situation, the virus and obviously supply and distribution are key, and so this would be each of you if I could get your response. You know, are you continuing to work with manufacturers to ensure an adequate domestic supply chain of medical countermeasures, and secondly, to improve the distribution of those medical countermeasures during the pandemic or moderate or severe seasonal flu epidemic like this year?

Dr. FRIEDEN. Absolutely, and I will let Dr. Goodman discuss more about the work with the manufacturers. We work with them by providing seed strains, and what our laboratories have been able to do is to optimize those seed strains so that there are strains that grow faster and that may be more effective when used in vaccines. So we are hoping to see kind of useful and important tweaks without huge breakthroughs yet in the flu vaccination. We also work through the strategic national stockpile in an emergency to provide vaccines, countermeasures and medications. What we found in the pandemic was that the vaccinations through the vaccines for children program could be scaled up enormously, so we were able to provide more than 300,000 shipments, more than 80 million doses very quickly, very effectively. We have been working to improve our ability to provide medications. Those are available but there isn't a system to get them out there, and one of the things that learned about emergencies is, it is best to have an everyday system that can be scaled up, so we are looking at some models of doing that even more effectively in the future.

Mr. HARPER. Thank you, Dr. Frieden.

Dr. Goodman?

Dr. GOODMAN. Yes, absolutely. We work extremely intensively with the manufacturers, and during flu season it is almost a daily contact with our staff scientists solving problems, working on issues, trying to get vaccine out quickly. I would also say through the Medical Countermeasure Enterprise across HHS, DOD, we are working together. Now FDA is involved at the earliest stages when the requirement for countermeasures is defined, and when requests for information or contracts go out to industry. The idea there is to avoid surprises, and spend as much effort as we can to increase the likelihood of success. So I think we are really helping keep that investment a very efficient and effective one.

Mr. HARPER. Thank you, Dr. Goodman.

Dr. Crosse, I am not meaning to ignore you but I am out of time, so I yield back.

Mr. MURPHY. I thank the gentleman. I now recognize the gentlelady from Florida, who is returning to the committee, Ms. Castor. Welcome.

Ms. CASTOR. Well, thank you very much, Chairman Murphy, especially for calling this very important hearing, and I want to thank our panel and experts for doing everything in your power to help Americans ward off the flu.

Before I get to my flu question, you know, when we are talking about the sequester, I think it is very important for everyone to remember, we have already slashed the budget of the CDC and the FDA. So when you are talking about additional draconian sequester cuts, you are not just asking the agency to be efficient because the agencies have been efficient and have cut. What you are doing is, you are cutting into their core missions that affect the productivity of Americans, our ability to ward off foodborne illnesses, SARS outbreaks. Think about the challenges with the flu. These things don't happen by magic. We have a responsibility to the American public and businesses to get them vaccinated, to get them all the tools they need to ward off disease, and I think it is just wishful thinking to say well, can you accept more budget cuts, more budget cuts, more budget cuts and not expect the core missions of these very important public health agencies to remain intact.

Back to the flu. In my home State of Florida, the nursing home population is critical, and the CDC has said that 90 percent of deaths from the flu come from people who are age 65 and older. This year, the flu has hit this population particularly hard. I am hearing more about how we are faring this season among that population, how effective our response has been and what we are doing to protect older Americans. So Dr. Frieden, can you talk about the impact of this season's flu on older Americans?

Dr. FRIEDEN. This year is an H3 year, and as in prior H3 years, it is more severe among the elderly. The hospitalization rate of laboratory-confirmed flu, which is something that provided in a graphic to the committee, is about twice or more what it has been in recent years, so overall this is a worse than average flu season and a particularly severe one for the elderly. Some of the things that we can do to reduce the severity is vaccination not only of seniors but if people around seniors so they are less likely to get infected by someone else, and then prompt treatment with a medication such as Tamiflu which particularly if given in the first 48 hours will reduce the likelihood of progression to severe disease. Also, in nursing homes, vaccination of health care workers is particularly important. There is some evidence that nursing homes that have lower vaccination rates among their staff have much worse outcomes in flu season.

Ms. CASTOR. And many of these long-term-care facilities, they just don't vaccinate their workforce like some hospitals do or cancer treatment centers. Why is that, and what can we do to promote greater vaccination rates among long-term-care employees?

Dr. FRIEDEN. We have seen steady progress in the proportion of health care workers getting vaccinated. It is currently slightly over 60 percent. It was in the mid 40s for many years. So we have seen progress and particularly among doctors, nurses and pharmacists.

We see rates of 80 to 90 percent. But working with nursing homes to make sure that vaccination is easy, provided, free on work time for their employees are all examples of things that are best practice and have been shown to be associated with higher rates. There are certainly nursing homes that do an excellent job at this, and so what we would like to do is see those best practices spread.

Ms. CASTOR. OK. In addition to increasing vaccination rates for long-term-care workers and many others, one of the keys to reducing the severity of seasonal flu is making sure that there is a good match between the strains in the vaccine and the strains of flu that are in circulation. Dr. Goodman, how well matched were the strains in this year's vaccine to what we saw circulating?

Dr. GOODMAN. Fortunately, the strains are very well matched this year, so that isn't an issue. The issue here is the severity of this virus, the number of unvaccinated people and then as we have discussed that we would like to have a vaccine that is even more effective, especially for the elderly.

Ms. CASTOR. So we had good matches this year. We didn't have any shortages in vaccines, even regionally?

Dr. GOODMAN. Well, we had good matches. There are times—what we always see is—it is sort of like whitewashing the fence. When there is bad flu around, people want the flu vaccine, and there is a lot of demand, so we have seen and CDC has helped manage situations where people might have transient difficulty locating vaccine but there is still vaccine available and people can still get vaccinated.

Ms. CASTOR. Well, I thank you all very much, and it is very important that we support our public health agencies so we can continue to minimize life-threatening illnesses and protect the productivity of American workers and businesses and protect the health of our families, so thank you very much. I yield back.

Mr. MURPHY. I thank the gentlelady for yielding back, and I will recognize another new member of the committee. The gentleman from Dr. Texas, Mr. Olson, is recognized for 5 minutes.

Mr. OLSON. I thank the chair, and welcome to the witnesses. Thank you all for your time and your expertise.

Just a little bit of background about myself. The district I represent is Texas 22. It is a suburban Houston district. That is ground zero for pandemic flu outbreaks, and we are about to be the third largest city in America. I want to apologize to my colleagues from Illinois, but Chicago is going to be number four pretty quickly. And we have the largest foreign tonnage port in America. That means traffic is coming from Asia, from Africa, from Europe, right there, the Port of Houston. We have got these huge transportation, land transportation infrastructure from Latin America, all the trucks, all the traffic coming across from Mexico right down Highway 59, which goes right to my district, which is now I-69. And while it is true that my hometown's minor league baseball team is called the Skeeters after mosquitoes, it is not true that the mosquito is the national bird of Texas. It is the mockingbird. But my point is, we have a lot of mosquitoes, we have a lot of rodents, a lot of birds, all sorts of transmission paths in addition to human beings, and while I thought that some of the comments that Dr. Burgess and Gene Green made about the outbreak we had, the

H1N1 outbreak in 2009, that summer we all know we had a big outbreak there across the country but Houston was number two, I think, of the national outbreak. And, I mean, 11 schools shut down and parents were terrified what was happening with their kids. And as you know, with these pandemic outbreaks, there are basically four steps we have to take care of. First we have to diagnose it. The CDC has to come through and say this is the virus, this is what it is, this is how we fix it. We have to make the vaccine. We have to get the vaccine manufactured out there and we have to get it to the people and have it delivered—I mean get it to the local people to deliver it to the people affected by disease. And it is pretty clear that outbreak in 2009, CDC got behind pretty quickly with all the tests being required, these people getting samples taken and all sent to you guys. I think you fixed that some, Dr. Frieden, by having some local regional centers set up to address this sort of explosion of tests. I also know we had big problems with delivery. I mean, you know, Texas Children's Hospital had to set up basically a drive-through in a parking garage because so many people wanted to come get those vaccines.

So my question is about the big picture, and this one is for you, Dr. Frieden, and for you, Dr. Goodman. What keeps you up at night? I mean, what is your base concern? What can we fix here? What is your biggest concern with our country dealing with these pandemic flu outbreaks?

Dr. FRIEDEN. So, of all of the naturally occurring infectious diseases, it is influenza that causes us to lose the most sleep because of its potential to kill. During the 1918 pandemic, more than 50 million people around the world died, and influenza can spread rapidly and unpredictably. One of the most predictable things about influenza is that it is unpredictable. So in order to do a better job of protecting Americans, we need to strengthen our global surveillance systems so that we can detect new strains of influenza soon after they arise anywhere in the world, and we have worked very closely with governments around the world as well as the World Health Organization to strengthen laboratories. In fact, during the H1N1 pandemic within literally days of the discovery of the virus, we had already produced a real-time PCR assay that we distributed ultimately to more than 100 countries around the world so we could track what was happening with it. But that virus was probably circulating for a couple of months before it was identified. So it emphasizes that if any part of the world doesn't have good monitoring systems, we could miss whether it is influenza or another health threat emerging and not be able to respond as quickly because if we can stop it or mitigate it where it emerges, that is better for that part of the world and that is better for us as well.

Mr. OLSON. There are some other institutions across America that do that. For example, the University of Texas medical branch in Galveston has its Bio 4 laboratory. I went and toured that thing. That is space age technology. They have these suits they dress you up in because they are dealing with some pretty serious diseases. They say exactly what you are saying, that our biggest problem is, we can find something somewhere in the world here. If we get the virus, we can probably have it done in 24 to 48 hours, they say. You know, we can figure out what the vaccine should be and they

have obviously got to manufacture it, but I would encourage you to work with them and all those different labs out there because they are great assets for us.

Dr. Goodman, what keeps you up at night, sir?

Dr. GOODMAN. Well, I think we are all sharing those same concerns of a new or different infectious agent where we don't have a great vaccine or great therapies that could occur either naturally or potentially deliberately. So, I agree totally with Dr. Frieden. We need to have strong surveillance, and things really have improved in that area too and the molecular tools.

I think we also need the next piece, which is the ability to develop and produce medical countermeasures—vaccines, drugs—much more quickly than we currently can. Normal drug development and vaccine development is a multiyear process. Among the things we are working with through our enterprise, HHS, DOD, etc., are new technologies to have a much more rapid, flexible response so that we can get vaccines much more quickly so that we can develop treatments. There also has been considerable progress as described in our testimony, in increasing our Nation's capacity and being sure we have the domestic capacity in the industrial infrastructure to work with the government and respond to a public health crisis. So again, we are better off, but we have got to harness new science to have much faster responses and be able to face a new threat. This effort isn't just for flu. It protects us from terrorism too. So for all of these, we are taking a multi-hazard approach where everything we do, whether it is surveillance or response, can be used because we can't predict what will emerge. We want tools that will work for whatever will emerge.

Mr. OLSON. Thank you. Dr. Crosse, you can sleep well at night, ma'am. That is the end of my questions. I do have some questions for the record, sir, about adjuvant vaccines are being used in Europe, sort of developing new technologies for vaccines. But thank you very much.

Mr. MURPHY. The gentleman yields back. The gentleman's time is expired, and we now recognize the gentleman from Virginia, Mr. Griffith, for 5 minutes.

Mr. GRIFFITH. Thank you, Mr. Chairman.

On these new vaccines that are being worked on, and it doesn't matter to me who answers the question or if people have different opinions. I am just curious, we know about the allergy problems for certain people with the eggs, but with the new vaccines that are done with cells, have there been any allergic reactions that we know of? Have there been any tests to see if folks that have other types of allergies are reacting to those vaccines?

Dr. GOODMAN. Well, the good news is that first of all, many people with egg allergies have safely taken the egg-based vaccines because they are fairly pure and they don't have tons of egg protein in them but there also are people who have had severe allergic reactions to the current vaccines, although it is extremely rare. For those who have them due to eggs, both the new recently approved vaccines should provide a potential advantage. One is produced in cells so there is no exposure to egg, and the other is produced in cells but using insect cells through recombinant technology, so these are very pure vaccines that don't contain egg protein. So I

think that will be a help. I want to get back to you for the record, but I am not aware of any significant problem with allergic reactions to either of the new vaccines other than what we would normally expect with any flu vaccine.

Mr. GRIFFITH. Thank you. With that, Mr. Chairman, if I can yield the remainder of my time to Dr. Burgess, I would do so.

Mr. BURGESS. I thank the gentleman for yielding.

Dr. Goodman and Dr. Frieden, at the end of 2005, an omnibus appropriations bill was passed that had the defense appropriations in it. A lot of the pandemic preparedness was contained therein and, again, going back to my opening statement, there was discussion about the universal vaccine. Dr. Frieden, you have talked about the difficulty with the surface proteins, how they are ever changing. I think, Dr. Goodman, you even mentioned developing a vaccine to the stalk or the housekeeping proteins that are contained within the coat. How close are we? This was one of the promises in 2005. It is 7 years ago.

Dr. GOODMAN. Well, I would—nature is very tricky, and as I said, this is a very crafty virus, so I would really hesitate to predict, but as I said, I think we see some promising science. I think the earliest we could begin to see something where we could maybe examine whether it has clinical benefit might be within 5 to 10 years. And that is if we see some of these technologies really take root, and I am excited about them, but I know my colleagues at NIH who also do this and fund this for a living, feel the same way. There are some exciting prospects but it has got a way to go. Certainly, you know, your support and the investments being made will help us get there faster, we hope.

You know, these are—we have wonderful vaccines against all kinds of infectious diseases. We protect children against pneumonia, against measles, against polio, et cetera. This is not for lack of trying. This is because this is a hard scientific problem. As I said, the human immune system does not respond very well to influenza, and when it does, the influenza virus is very tricky at getting away from that response.

Mr. BURGESS. Well, is a universal vaccine still a worthwhile goal?

Dr. GOODMAN. Still a goal?

Mr. BURGESS. A universal vaccine, is that still—

Dr. GOODMAN. Is it a worthwhile goal?

Mr. BURGESS. I am asking you, is it a worthwhile goal?

Dr. GOODMAN. Absolutely, absolutely. I mean, can you imagine if we could have a world where we didn't have influenza pandemics?

Mr. BURGESS. You can just imagine, though, the frustration in 2005 we are told we are 3 to 5 years away. You are telling me now we are 7 to 10 years away, and it—

Dr. GOODMAN. Well, I don't think I would have said that and I am not sure who did but I think, you know, we see new technology and we are always very hopeful, and it is kind of the way you go in science is to be optimistic and pursue the best leads, but one of the things we also certainly have seen is, this is a very challenging scientific problem.

Mr. BURGESS. Well, let me ask you this. We got a good match this year so we are grateful for that. But still, the prevalence of in-

fections in those over the age of 65 is still higher, so what is the difficulty there in conferring the advantage to the individual over 65?

Dr. FRIEDEN. One of the challenges with influenza is that our own natural immunity isn't particularly good, and vaccines don't usually do better than we do in nature in defending against infections. The elderly, particularly the frail elderly, who are more susceptible to severe flu, don't in the past respond very well to the flu vaccine. There is a new product on the market that uses triple doses of the antigen. We are told by the manufacturer that by the end of next flu season we will be able to get a sense of whether that makes a difference or not. But influenza is one of the things that is quite challenging. Ninety percent or more of the deaths in most years tend to be among the elderly, so one of the things that we can do is vaccinate more people around them to tamp down the threat of flu. A second is to treat promptly because there is evidence that if you treat someone within the first 48 hours, they are less likely to end up in the intensive care unit and it may have other benefits as well in reducing spread.

Mr. BURGESS. Very good. I yield back.

Ms. DEGETTE. Mr. Chairman, I ask unanimous consent for 30 seconds to follow up on that question.

Mr. MURPHY. Without objection.

Ms. DEGETTE. So the follow-up question, Dr. Goodman, is—and by the way, it was the CDC apparently in this 2005 hearing that said it was 3 to 5, and it wasn't Dr. Frieden that said that.

Dr. Goodman, this universal vaccine 5 to 10 years that you said, if we wanted to speed that up, is that a resource question or is it a science question, or both?

Dr. GOODMAN. I think at this point it is mostly a science question, to be honest.

Mr. MURPHY. Thank you. The Chair recognizes now the gentleman from Ohio, Mr. Johnson, for 5 minutes.

Mr. JOHNSON. Well, thank you, Mr. Chairman, and first of all, let me say what a privilege and an honor it is to now be a part of the Oversight and Investigations Subcommittee. I look forward to serving with all of our colleagues as we address the many important issues that face us.

And with that, let me say I received my flu vaccine this year and I have not gotten sick yet, so for those involved, thank you very much. I am very much appreciative.

I represent a district in Ohio that is extremely rural. It takes me 6½ hours to drive from one end to the other. There are many places throughout my district where my constituents have to drive 30, 40 miles to get to a physician or to get to a pharmacy or to get to a flu shot if they were to have a reaction. So this is, and especially given your testimony already, impacting our seniors, and I have a lot of seniors down in that area.

So Dr. Goodman, can you explain a little bit more about the testing process in place to verify the safety, the sterility and the effectiveness of the vaccine?

Dr. FRIEDEN. So, as part of each manufacturer's approval or license, they are required to do numerous tests throughout the vaccine manufacturing. At multiple stages they have to monitor pro-

duction. And then when they create these large-scale bulk amounts of vaccine, those are all tested for their potency, their sterility to be sure there is no contaminants, toxins, etc. In addition, they submit samples of that to FDA, which our laboratories test, and then once all those tests are OK, they fill the vaccines into the final containers or the syringes or for the live vaccine, FluMist, the nasal spray, and they also test where appropriate those final formulations. So there is very extensive testing and quality control, among the most intense, I would say, for medical product.

The other thing that we do that is very important is working closely with CDC. We monitor the safety of all licensed vaccines very carefully, and this is particularly true of influenza vaccine. We monitor for major side effects in real time using, for example, the CMS database, and this is actually some of the most novel science done in looking for adverse events, and we are working to stand up a much broader system that uses health care settings that have electronic medical records to monitor vaccine safety called Prism, and we plan to have that up and running next year. So they are very intensively monitored, and I would say one of the way our country was able to do a good job with vaccine uptake in the 2009 pandemic is that we were able to track safety in real time when the public or certain people raised concerns about the safety of vaccine to be able to share the data which showed it was safe. Conversely, if there ever were, God forbid, to be a problem, we think we have support and test systems in place to detect it rapidly.

Mr. JOHNSON. Sure. Do you think that the development time for the vaccine, because it seems to get longer and longer each year as the virus mutates, is harming our ability to react to a potentially strong flu season?

Dr. GOODMAN. You know, the manufacturing of flu vaccine is complicated, and as Dr. Frieden said, flu is unpredictable. We also say flu vaccine manufacturing is unpredictable. Sometimes the viruses grow better than other years. Sometimes they yield more of the vaccine material than other years, so it can be a challenge. This year went relatively smoothly. We have had other years where vaccine is delayed. Typically, it is about a 6-month process beginning to end. We are all working to speed that up. There are parts the virus controls like how it grows, and that is what got us in the pandemic. The virus just wouldn't grow. But there are parts that we can help control better. We recently approved rapid sterility tests that instead of taking 2 weeks take 3 to 5 days. We are working with CDC and others to make better potency tests, which now take weeks to develop, and we think we can shorten that. So we are working to shorten the portion of the time that manufacturers and the regulatory agencies are responsible for but we are at the end left with the whim of the virus, which is why some of these new technologies, like cell-based and recombinant, may provide us with a safety valve if problems occur.

Mr. JOHNSON. One quick question before my time expires, which is almost here. Again, given my rural district, I am sure there must be scientific formulas to determine the distribution of the vaccine to make sure that you have got them in the right places so the population can get to them. I am sure there is a different methodology

for a big city like Columbus or Cleveland or Los Angeles than for rural Appalachia Ohio.

Dr. FRIEDEN. We work closely with public and private sectors to make sure that vaccine is available. Other than some spot shortages, it generally was this year, and using community providers, senior centers, pharmacies and other places, any opportunity to provide vaccination—many States allow pharmacists, nurses, nurse practitioners to vaccinate under a doctor's order or supervision—can increase access in rural and other areas.

Mr. JOHNSON. Thank you, Mr. Chairman. I yield back.

Mr. MURPHY. I thank the gentleman. I also forgot to mention welcome to the committee to you, to the gentleman who represents the east coast of Ohio. I appreciate it.

Mr. JOHNSON. Yes, the very long east coast.

Mr. MURPHY. Now I recognize another new member to our subcommittee, the gentlelady from North Carolina and a nurse. Ms. Ellmers is recognized for 5 minutes.

Mrs. ELLMERS. Great. Thank you, Mr. Chairman, and again to our panel, thank you for being here and answering our questions.

I happen to be the lucky recipient of the district that has Novartis, the new, beautiful, gorgeous Novartis facility in Holly Springs, North Carolina, and so my questioning is along the lines of what they are going to be able to do. My first question, Dr. Frieden, for you is, you know, considering now the advancements and how exciting it is that we are taking the path of new technologies in vaccinations, how is it and how can you describe to us the demanding or expanding the demand for facilities like this, manufacturing, can be a help in this area? Because we are looking for solutions moving forward—how can this facility be a step in that right direction?

Dr. FRIEDEN. Well, as you know, the cell-based manufacturing offers advantages, possibly cutting a few weeks or even a month out of the time frame, not using eggs, and having one more option, and one of the things that has been encouraging in recent years is the increased number of options—intradermal vaccination, intranasal vaccination, high-dose vaccination for seniors. So the more options we have, I think the more uptake we will have. But we would like to see a substantial increase in uptake of influenza vaccination, and that is going to require continued effort.

We do really well with childhood vaccination in this country through the Vaccines for Children program, where we provide about half of all the vaccines that are used. Not only do we have very high rates but we have eliminated racial and ethnic disparities in childhood vaccination. But we don't do nearly as well for adolescents and adults, and part of that is putting in place systems in our health care that make it routine, that put frankly nurses in charge rather than doctors to make sure that something gets done regularly and routinely.

Mrs. ELLMERS. I am all about that. A little competition doesn't hurt.

Along that line, and I know Dr. Goodman touched on this as well, what is the advantage, if you will, speaking to the cell-based vaccines versus the egg? Of course, we all know about egg allergies, but I know you had mentioned, you know, the rapid, you know,

rate that we can be manufacturing and growing, so can you just touch on a couple of those as well?

Dr. FRIEDEN. So not being reliant on eggs is quite important because you might have a shortage of eggs in the case of a pandemic, so that is an important advance. As Dr. Goodman mentioned, the egg allergy issue is less of an issue because we find that true egg allergy is extremely rare, and we have not generally seen problems. In fact, we have clarified our recommendations in the past year to say really it has to have been a real severe anaphylactic allergy because we found many people saying well, I don't like eggs so I am not going to have the flu vaccine.

Mrs. ELLMERS. A fear factor?

Dr. FRIEDEN. Right.

Mrs. ELLMERS. Dr. Goodman, I did want to ask, in this particular facility, the Novartis facility, it is licensed now for the pandemic vaccine but not yet licensed for the seasonal. Is that correct?

Dr. GOODMAN. I have to be careful about public information versus their protected information.

Mrs. ELLMERS. I see.

Dr. GOODMAN. But it is licensed for certain operations with respect to flu vaccine. It is not finally licensed for production of seasonal vaccine, and I know Novartis is working with our staff to get it going and get it onboard, and that is their plan.

Mrs. ELLMERS. In a facility like this, how long would something like this take? And there again, I will just say hypothetically for other facilities that may have taken that plan.

Dr. GOODMAN. Yes, it sort of depends on the issues encountered and, you know, I know that there is really highly interactive engagement and everybody's goal is to get it going as soon as possible, and you know, things have been going well.

Mrs. ELLMERS. Good. And what I will say is, any help that we can be in that effort, I will be more than——

Dr. GOODMAN. No. As I said, the relations between FDA and with manufacturers in this area have been tremendous and very collaborative.

Mrs. ELLMERS. Excellent. Well, thank you so much. I thank all of you so much for your input, and I yield back.

Mr. MURPHY. I thank the gentlelady for yielding back. We have covered all of the members here. I just want to cover a couple of——

Ms. DEGETTE. Will the gentleman yield for 1 second? Mr. Chairman, I just want to congratulate you on your first hearing, and I want to congratulate all of the members for the comity that we have shown. This is an important issue, and I really appreciate the bipartisan cooperation and I think you are setting the tone for a really good 113th Congress. I just wanted to compliment you.

Mr. MURPHY. I thank the gentlelady, and the same compliments go to the ranking member and all the members here. To those who testified today, we know this is a serious topic, and I know our hearts go out to all those families across America who lost loved ones during this flu epidemic, but the information you are providing, the research you are providing and recommendations for the future are going to be critically important to save more lives next year, and so we are looking forward to that.

A couple housekeeping matters. I do ask unanimous consent that the written opening statements of members will be introduced into the record. Without objection, the documents will be entered into the record.

Again, I thank the witnesses for coming today and for their testimony and members for their devotion to this hearing. The committee rules provide that members have 10 days to submit additional questions for the record to the witnesses.

This was my first hearing as chairman of the subcommittee, and I appreciate all the constructive and bipartisan dialog that we have had. When problems or issues arise that impact our public health, I am committed to finding out how we can effectively address them, and the FDA is going to continue to play a critical role in this regard.

Dr. Goodman, I do have a request if you would do this for us, to take back to the Commissioner, Commissioner Hamburg. As you know, the committee has investigating the deadly outbreak of fungal meningitis linked to compound drugs since October. Almost 2 weeks ago, this committee sent Dr. Hamburg and notified her that unless all responsive documents are produced by February 25, the committee will move to compel their production. We have not received any documents since the day we sent the letter. Dr. Goodman, could you please on behalf of this committee tell the Commissioner we expect the FDA's cooperation, and the only way for HHS to avoid receiving a subpoena in the meningitis investigation is to produce all the documents we have requested by the February 25th deadline. I thank you for taking that message back to the FDA Commissioner.

With that, I thank all the members. This hearing is adjourned.
[Whereupon, at 11:52 a.m., the subcommittee was adjourned.]

